Library, N.W. Bldg
DEC 1 3 1961
Reference book not to be taken from the library.

A MANUAL OF RADIOACTIVITY PROCEDURES

Handbook 80

U.S. Department of Commerce
National Bureau of Standards

HANDBOOKS OF THE NATIONAL BUREAU OF STANDARDS

The following Handbooks are available by purchase from the Superintendent of Documents, Government Printing Office, Washington 25, D.C., at the prices indicated:

No.		Price
28	Screw-Thread Standards for Federal Services 1957, Part I (Amends in part H28 1944 and in parts its 1950 Supplement)	$1. 25
28	Screw-Thread Standards for Federal Services 1957, Part II	. 75
28	Screw-Thread Standards for Federal Services 1957, Part III	. 60
30	National Electrical Safety Code	2. 25
42	Safe Handling of Radioactive Isotopes	. 20
44	Specifications, Tolerances, and Regulations for Commercial Weighing and Measuring Devices—2d Edition	2. 00
48	Control and Removal of Radioactive Contamination in Laboratories	. 15
49	Recommendations for Waste Disposal of Phosphorus-32 and Iodine-131 for Medical Users	. 15
50	X-ray Protection Design	. 20
51	Radiological Monitoring Methods and Instruments	. 20
53	Recommendations for the Disposal of Carbon-14 Wastes	. 15
55	Protection Against Betatron-Synchrotron Radiations up to 100 Million Electron Volts	. 25
57	Photographic Dosimetry of X- and Gamma Rays	. 15
58	Radioactive-Waste Disposal in the Ocean	. 20
59	Permissible Dose From External Sources of Ionizing Radiation	. 35
63	Protection Against Neutron Radiation up to 30 Million Electron Volts	. 40
64	Design of Free-Air Ionization Chambers	. 20
65	Safe Handling of Bodies Containing Radioactive Isotopes	. 15
66	Safe Design and Use of Industrial Beta-Ray Sources	. 20
67	Checking Prepackaged Commodities	. 35
68	Tabulation of Data on Receiving Tubes	1. 00
69	Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure	. 35
72	Measurement of Neutron Flux and Spectra for Physical and Biological Applications	. 35
73	Protection Against Radiations from Sealed Gamma Sources	. 30
74	Building Code Requirements for Reinforced Masonry	. 15
75	Measurement of Absorbed Dose of Neutrons and of Mixtures of Neutrons and Gamma Rays	. 35
76	Medical X-Ray Protection up to Three Million Volts	. 25
77	Precision Measurement and Calibration	
	Vol. I. Electricity and Electronics	6. 00
	Vol. II. Heat and Mechanics	6. 75
	Vol. III. Optics, Metrology, and Radiation	7. 00
78	Report of the International Commission on Radiological Units and Measurements, 1959	. 65
79	Stopping Powers for Use with Cavity Chambers	. 35
80	A Manual of Radioactivity Procedures	. 50

U.S. Department of Commerce, Luther H. Hodges, Secretary
National Bureau of Standards, A. V. Astin, Director

A Manual of Radioactivity Procedures

Recommendations of the
National Committee on Radiation Protection
and Measurements
NCRP Report No. 28

National Bureau of Standards Handbook 80
Issued November 20, 1961

For sale by the Superintendent of Documents, Washington 25, D.C. - Price 50 cents

Foreword

As a result of obvious needs in the field of radiological measurements, the National Committee on Radiation Protection and Measurements in 1956 established three new subcommittees to deal with such problems. The present report has been prepared by the Subcommittee on Standards and Measurements of Radioactivity for Radiological Use. Upon direction by the Main Committee, this report presents a survey of the practice of radioactivity measurement with special reference to clinical and biological applications. It also includes some guidance as to procedures to be followed in radioactivity assays which would be of help to those who are embarking upon careers as hospital physicists or who may be confronted with the task of establishing a radiation physics department in a hospital or medical institution.

The substance of this report is not designed to meet some of the large-scale problems encountered in the heavy nuclear industry.

A. V. Astin, *Director.*

Preface

Because of the nature of the problems encountered in clinical radiology, it appeared desirable to divide the preparation of this manual into three parts, the first part dealing with basic standardization procedures which was prepared under the chairmanship of Dr. K. W. Geiger. The second and third parts, dealing with specialized clinical and biological applications, were prepared under the chairmanship of Dr. W. K. Sinclair. There has been a substantial intermingling of responsibility between the two groups and it is hoped that the overall manual is presented in a sufficiently uniform style. In view of the similarity of the problems and the procedures that exist in the two countries, the membership of this subcommittee and its task groups was comprised of representatives from laboratories in both Canada and the United States.

In addition to the recommendations contained in this manual, the members of the Subcommittee would like to draw to the attention of its readers a number of texts that will be found to be of particular value in many areas in the clinical application of radioactive materials. These texts are listed in the General References at the end of this manual. In some cases references in the text may appear only under General References (e.g., an NCRP–NBS Handbook). It is therefore suggested that an abortive search in the References section should be followed by a perusal of the short General References section.

The following are members of either the subcommittee or one of its task groups:

W. B. Mann, Chairman*
P. J. Campion
L. M. Cavallo
C. L. Comar
T. P. Eberhard*†
E. W. Emery
S. Feitelberg
S. B. Garfinkel
K. W. Geiger*
W. Gross*
J. Hale
R. W. Hayward
W. F. Marlow
E. H. Quimby
S. A. Reynolds
R. Rugh*
H. H. Seliger
W. K. Sinclair*
H. O. Wyckoff
W. J. Youden

*Members of Subcommittee M–1.
†Deceased

The following parent organizations and individuals comprise the main committee:

Barnes, E. C., Am. Indust. Hygiene Assoc.
Barnes, C. M., Am. Vet. Med. Assoc.
Braestrup, C. B., Radiol. Soc. of North America and Subcommittee Chairman.
Brennan, J. T., Col., U.S. Army.
Bruce, F. R., Am. Nuclear Soc.
Bugher, J. C., Representative-at-large.
Chamberlain, R. H., Am. College of Radiology.
Claus, W. D., USAEC.
Crow, J. F., Representative-at-large.
Doan, R. L., Am. Nuclear Society.
Dunham, C. L., USAEC.
Evans, T. C., Am. Roentgen Ray Soc.
Failla, G., Representative-at-large.
Focht, E. T., Am. Radium Soc.
Gorson, R. T., Subcommittee Chairman.
Healy, J. W., Health Physics Soc. and Subcommittee Chairman.
Hodges, P. C., Am. Medical Assoc.
Keene, A. R., Subcommitte Chairman.
King, E. R., Capt. U.S. Army.
Kleinfeld, M., Intern. Assoc. of Govt. Labor Officials.
Koch, H. W., Subcommittee Chairman.
Livermore, D. I., Lt. Col. ,U.S. Air Force.
LeRoy, G. V., Subcommittee Chairman.
Mann, W. B., Subcommittee Chairman.
McAdams, W. A., Atomic Indust. Forum and Subcommittee Chairman.
Morgan, G. W., Subcommittee Chairman.
Morgan, K. Z., Health Phsyics Soc. and Subcommittee Chairman.
Muller, H. J., Genetics Soc. of America.
Nelsen, R. J., Am. Dental Assoc.
Newell, R. R., Am. Roentgen Ray Soc.
Norwood, W. D., Indus. Medical Assoc.
Parker, H. M., Subcommittee Chairman.
Powell, C., USPHS.
Reeves. J. D., Am. College of Radiology.
Reynolds, J. A., Natl. Elec. Mfgr. Assoc.
Rossi, H. H., Subcommittee Chairman.
Robbins, R., Am. Radium Soc.
Shipman, T. L., Indust. Med. Assoc.
Skaggs, L. S., Subcommittee Chairman.
Stern, Curt, Genetics Society of America.
Sterner, J. H., Am. Indus. Hygiene Assoc.
Stone, R. S., Radiological Society of North America.
Taylor, L. S., National Bureau of Standards.
Trout, E. D., Nat. Elec. Mfgr. Assoc.
Trum, B. F., Am. Vet. Med. Assoc.
Warren, Shields, Representative-at-large.
Weatherwax, J. L., Representative-at-large.
Williams, E. G., Representative-at-large.
Wyckoff, H. O., Subcommittee Chairman.

The following are the subcommittees and their chairmen:

Subcommittee 1. Permissible Dose From External Sources, H. M. Parker.
Subcommittee 2. Permissible Internal Dose, K. Z. Morgan.
Subcommittee 3. X-rays up to Three Million Volts, R. G. Gorson.
Subcommittee 4. Heavy Particles (Neutrons, Protons, and Heavier), H. H. Rossi.
Subcommittee 5. Electrons, Gamma Rays, and X-rays Above Two Million Volts, H. W. Koch.
Subcommittee 6. Handling of Radioactive Isotopes and Fission Products, J. W. Healy.
Subcommittee 7. Monitoring Methods and Instruments, A. R. Keene.
Subcommittee 8. Waste Disposal and Decontamination. (This subcommittee has been inactivated.)
Subcommittee 9. Protection Against Radiations From Radium, Cobalt-60, and Cesium-137 Encapsulated Sources, C. B. Braestrup.
Subcommittee 10. Regulation of Radiation Exposure Dose, W. A. McAdams.
Subcommittee 11. Incineration of Radioactive Waste, G. W. Morgan.
Subcommittee 12. Electron Protection, L. S. Skaggs.
Subcommittee 13. Safe Handling of Bodies Containing Radioactive Isotopes, E. H. Quimby.
Subcommittee 14. Permissible Exposure Doses Under Emergency Conditions, G. V. LeRoy.
Subcommittee M–1. Standards and Measurement of Radioactivity for Radiological Use, W. B. Mann.
Subcommittee M–2. Standards and Measurement of Radiological Exposure Dose, H. O. Wyckoff.
Subcommittee M–3. Standards and Measurement of Absorbed Radiation Dose, H. O. Wyckoff.
Subcommittee M–4. Relative Biological Effectiveness, V. P. Bond.

Lauriston S. Taylor, *Chairman.*

Contents

	Page
Foreword	III
Preface	IV
Part I. Radioactivity standardization procedures	1
1. Introduction	1
1.1. Units and definitions	1
1.2. General procedures for absolute standardization	3
1.3. Supply of radioactive materials	4
1.4. Chemical considerations in preparation, storage, and distribution of radioactive solutions	5
2. Physics of some radiation detectors	5
2.1. Ionization chambers	5
2.2. Proportional counters	8
2.3. Geiger-Müller counters	13
2.4. Scintillation counters	14
2.5. Statistics and precision of measurements	25
3. Principal methods for absolute standardization	29
3.1. Standardization by 4π counting	29
3.2. Coincidence counting	36
3.3. Standardization by internal gas counting	42
3.4. Calorimetric method	42
3.5. Liquid scintillation counting	43
3.6. Standardization of gamma emitters by dosimetry	44
3.7. Standardization of beta emitters by dosimetry	51
3.8. Loss-of-charge method	52
3.9. Calculation of activity of artificially produced radionuclides from irradiation data	53
4. Methods of relative standardization as carried out in standardization laboratories	54
4.1. General	54
4.2. Ionization chambers	55
4.3. Solution counting	56
4.4. Liquid scintillation counting	57
4.5. Gel scintillation counting	57
5. Techniques of preparing standard solutions and samples for counting	58
5.1. Standard solutions	58
5.2. Dry samples	58
5.3. Gas samples	62
5.4. Liquid samples	63
Part II. Measurement of radioactivity for clinical and biological purposes	64
6. Introduction	64
7. Instruments used in relative standardization	66
7.1. General	66
7.2. Ionization-current-measuring systems	67
7.3. Counting systems	73
7.4. Geiger-Müller counters	76
7.5. Proportional counters	76
7.6. Scintillation counters	77
7.7. Use of standards and reference sources	81

Part II. Measurement of radioactivity for clinical and biological purposes—Continued Page
8. Preadministration sample measurement 82
8.1. General 82
8.2. Radioactivity assay methods 83
8.3. Radionuclide identification 85
8.4. Chemical purity and pyrogen activity 86
8.5. Measurement of dose rate from small sealed sources for direct application 86
9. *In vivo* measurement—quantitative studies 88
9.1. General 88
9.2. Measurement of iodine-131 uptake in the thyroid gland 91
9.3. Quantitative estimations in organs other than the thyroid 95
9.4. Estimation of whole-body radioactivity in humans and animals 96
10. *In vivo* counting methods—distribution studies 100
10.1. General 100
10.2. Manual scanning 101
10.3. Automatic scanning 102
10.4. Interpretation of scans 109
11. *In vivo* counting methods—time studies 110
11.1. General 110
11.2. Studies in which the radionuclide is injected directly into the bloodstream 111
11.3. Studies in which the radionuclide is injected directly into a tissue 112
11.4. Background 113
12. Measurement of postadministration samples 113
12.1. General 113
12.2. Sample preparation 114
12.3. Calibration techniques 116
12.4. Gamma-ray sample assay 116
12.5. Beta-particle sample assay 118
12.6. Paper chromatography and paper electrophoresis 120
12.7. Autoradiography 125
Part III. Disposal of radioactive materials 131
13. Disposal procedure 131
13.1. Disposal limits 131
13.2. Determination of permissible disposable quantity 133
13.3. Measurement of disposal amounts 135
Appendixes
A. Nuclear decay data for radionuclides which may be useful in medicine 137
B. Preferred methods of measurement for clinical and biological purposes 141
C. Measurements necessary in diagnostic techniques 143
D. Measurements necessary in therapeutic techniques 144
14. General references 145
15. References 146

A Manual of Radioactivity Procedures

PART I. Radioactivity Standardization Procedures

1. Introduction

1.1. Units and Definitions

Radioactivity is the outward manifestation of the spontaneous transformations of *radioactive* nuclei.

A *nuclide* is any individual nuclear species, such as C^{12}, C^{14}, P^{32}, I^{131}, etc., irrespective of whether or not the *nuclide* has other *isotopes*. The term *isotope* is frequently misused nowadays for *nuclide* but the strict meaning of the former as originally defined by Soddy [1914] is *of the same place;* i.e., in the same position in the periodic table. Thus one may say that the *nuclide* phosphorus-32 is an *isotope* of phosphorus, or even more specifically of, say, phosphorus-33. A radioactive nuclide is often referred to as a *radionuclide.*

The strength of radioactive material can be expressed in a number of ways. For example one may specify the strength or activity, at any given time, in disintegrations per unit time. The activity has the dimension second^{-1} and is often expressed in curies.

The *curie* is defined by international agreement [Paneth, 1950] as the quantity of any radioactive material in which the number of disintegrations is 3.700×10^{10} per sec.

The unit of exposure of X or gamma radiation is the *roentgen.* One roentgen is an exposure of X or gamma radiation such that the associated corpuscular emission per 0.001293 g of air produces, in air, ions carrying 1 electrostatic unit of quantity of electricity of either sign.

The *specific gamma-ray emission* of a radioactive nuclide is the exposure dose rate produced by the unfiltered gamma rays from a point source of a defined quantity of that nuclide at a defined distance.

The unit of specific gamma-ray emission is the *roentgen per millicurie hour at 1 cm* (r/mc-h at 1 cm or $\text{r-cm}^2/\text{mc-h}$).

While the disintegration rate at a given time of a radionuclide may be measured directly, it can also be derived from a knowledge of the number of radioactive nuclei present at that time and their half-life. The strength of a source may also be expressed in terms of such quantities as the rate of energy release or of the exposure dose rate at a given distance. The disintegration rate may then be derived from these quantities provided that the average energy per disintegration or decay scheme of the nuclide is known.

A *standard* is a preparation of known strength. When such a standard has been calibrated in terms of the accepted standards of mass, length, and time, it is said to have been determined in *absolute measure*. Such a standardization is known as an *absolute standardization* and the standard is often called an *absolute* or *primary* standard. Such absolute measurements may have been made in a national laboratory or elsewhere. It has recently been proposed [McNish, 1958 and 1960], however, that such standards of a national or international character be designated *national standards* or *international standards* respectively.

A *relative* standard (or, as it is sometimes called, a *derived* or *secondary* standard) is one which has been calibrated in terms of one whose value has been determined in *absolute measure*. Many standards are commercially available and may be used to calibrate routine measuring equipment. This equipment may then be used to calibrate those radioactive preparations which the user employs for his task; these latter may be called *working, laboratory,* or *calibration standards*.

In some cases it is feasible to replace short-lived standards by *simulated standards* which consist of a mixture of longer-lived radionuclides. Over a substantial part of the energy spectrum, and usually for a limited time, these simulated standards have almost identical radiation characteristics to the short-lived radionuclide they replace.

The expression *reference source* or *performance standard* designates a long-lived radioactive source, the actual strength of which does not need to be known. This type of source is used to check the constancy of radiation-detecting equipment. Such equipment in conjunction with a long-lived reference source, such as radium, may, after calibration with a standard of a short-lived radionuclide, actually constitute a user's laboratory or working standard of that short-lived radionuclide. Even in many national standardizing laboratories this combination of equipment, in the form of ionization chambers and long-lived sources, constitutes the national standard of a short-lived radionuclide.

The terms *accuracy* and *precision* are used in the following sense. *Accuracy* expresses the degree of agreement with the true value of the quantity being measured and is subject to the influence of unknown systematic errors. *Precision* expresses the degree of reproducibility of measurements. The standard deviation of a set of measurements is often used as the criterion of precision. (For more detailed definitions of these items, Kendall and Buckland, 1957, may be consulted.)

1.2.1. *Measurement of disintegration rate.* The most frequently used technique for absolute standardization involves the direct measurement of the disintegration rate of the source. In principle this can be achieved by a suitable radiation counter subtending a fixed and known solid angle at the source. The detection efficiency for the particular source spectrum has to be known and corrections for radiation scattering and absorption need to be applied. Detection efficiencies may be determined by the method of coincidence counting provided the decay scheme is known. For charged-particle emitters a considerable simplification can be achieved by using a windowless counter subtending a solid angle of 4π around the source, since this not only makes the geometrical factor unity but also eliminates all corrections for scattering and absorption outside the source. For very thin sources and charged particles of not too low an energy, practically 100-percent detection efficiency can be obtained.

The following methods may also be considered as "near-absolute" methods of standardization. In these methods the disintegration rate is not measured directly, but if certain data on the decay or production of the radionuclide are known, the disintegration rate can be calculated.

1.2.2. *Weighing of a radioactive element.* Historically weighing is the oldest method of standardization, having first been applied in the case of radium in 1911. This radium, which was used to determine the atomic weight of radium-226, was considered to be isotopically pure. Weighing, or its equivalent, such as measuring the pressure, volume and temperature of a gas, may also be used to determine the activities of radioactive nuclides, provided that the isotopic abundance of the nuclide in question and its decay constant are known. The disintegration rate, dN/dt can then be determined as it is given by the radioactive decay law

$$\frac{dN}{dt}=-\lambda N, \tag{1}$$

where λ is the decay constant ($\lambda T=\ln 2$, T=half-life) and N is the number of unstable nuclei, determined by weighing, or its equivalent.

1.2.3. *The calorimetric method.* Particularly suitable for short-range particle emitters (such as alpha or low energy beta) is the calorimetric method in which the rate of energy emission from the radioactive substance is measured. The conversion to activity requires a knowledge of the average energy per disintegration.

1.2.4. *Ionization measurements.* If the average energy expended by radiation in forming one ion pair in a gas be known, the total energy of the radiation from a source can be determined from ionization-current measurements. The determination of the activity of the source then requires a knowledge of the average radiation energy emitted per disintegration, for the nuclide in question.

1.2.5. *Loss-of-charge method.* For charged-particle emitters the loss-of-charge method allows the number of such particles emitted to be calculated from a measurement of the charge transfer. Since the method is rather insensitive it is not recommended for practical use.

1.2.6. *Activity from production data.* Knowledge of the irradiation data and production cross section for artificially produced radionuclides allows a fair estimate of the activity.

1.2.7. *Summary.* Table 1.2–1 shows the conversion formulas giving disintegration rates in terms of various measured quantities for different methods.

TABLE 1.2–1. *Conversion of various measures of radioactivity into disintegrations per second*

Strength of radioactive nuclide expressed as	Disintegrations per second	Remarks
1 curie	3.700×10^{10}	
1 gram of pure radioactive nuclide	$\frac{6.025\times10^{23}}{A}\lambda$	λ decay constant (sec^{-1}), A atomic weight (physical).
1 watt total rate-of-energy emission	$\frac{6.24\times10^{12}}{\bar{E}}$	$\bar{E}$ average energy emitted per disintegration (Mev).
1 roentgen/hour at 1 cm (from gamma-emitting point source).	$\frac{3.700\times10^{7}}{\Gamma}$	For values of Γ, the specific gamma-ray emission, see appendix A.
1-microampere charge loss	$\frac{6.24\times10^{12}}{p}$	p number of electron charges emitted per disintegration.

1.3. Supply of Radioactive Materials

Radioactive materials are produced by neutron bombardment, usually in a reactor, or bombardment with charged nuclear particles in a cyclotron or other accelerator. Some radioactive materials are also available as fission products from reactors. Radionuclides which occur in nature can be isolated by appropriate methods.

Artificial and naturally occurring radionuclides and also stable nuclides can be obtained from various organizations whose catalogs should be consulted for detailed lists and descriptions of materials and services furnished. A comprehensive purchasing guide, The Isotope Index, is published yearly by the Scientific Equipment Co., Indianapolis 19, Ind.

1.4. Chemical Considerations in Preparation, Storage, and Distribution of Radioactive Solutions

It is important that radioactive solutions should be chemically and physically stable. In some cases, an inactive material, isotopic with the radionuclide, or in the same periodic group, is added as a "carrier" to prevent or minimize adsorption effects and "radiocolloidal" behavior [Hahn, 1936]; in other cases, this can be done simply by increasing the hydrogen ion concentration of the solution. A radionuclide should be present, if possible, in simple ionic form to permit it to exchange readily with its carrier element (whether isotopic or not), or to follow its expected chemistry [Friedlander and Kennedy, 1955]. There are elements, such as gold, which must be handled in the form of complexes to insure stable solutions. However, many simple salts of elements, such as NaCl, are chemically stable in simple acid solution. In table 1.4–1 are found examples of the types of solutions employed (see also sec. 5.1).

TABLE 1.4–1. *Compositions of typical radionuclide solutions* [a]

Radionuclide	Compound	Solution
P-32	H_3PO_4	$<0.5\ N$ HCl
S-35	H_2SO_4	$\sim 0.1\ N$ HCl
S-35	BaS	$\sim 0.15\ N$ $Ba(OH)_2$
S-35	S	Benzene
Se-75	H_2SeO_3	$1\ N$ HCl
As-76	$HAsO_2$	$1\ N$ HCl
Br-82	KBr	$1\ N$ HCl
Zr-95	Complex	$\sim 0.5\%$ $H_2C_2O_4$
Nb-95	Complex	5% $H_2C_2O_4$
Tc-99	NH_4TcO_4	$1\ N$ NH_4OH
Sb-122	$SbCl_3$+SbOCl	$1\ N$ HCl
I-131	NaI	Na_2SO_3+NaOH
Hf-181	$HfOCl_2$	$1\ N$ HCl
Re-186	$HReO_4$	$1\ N$ HNO_3
Ir-192	Na_2IrCl_6	$0.1\ N$ HCl
Au-198	$AuCl_3(HAuCl_4)$	$1\ N$ HCl+HNO_3
Bi-210	$Bi(NO_3)_3$	$1\ N$ HNO_3

[a] From "Radioisotopes Catalog and Price List," Oak Ridge National Laboratory.

2. Physics of Some Radiation Detectors

2.1. Ionization Chambers

An ionization chamber is an instrument in which an electric field is applied across a volume of gas. Charged particles moving through matter undergo inelastic collisions with atoms or molecules. In a gas, these particles form positive ions and electrons which, in the absence of an electric field,

will recombine. In some gases the electrons may become attached to neutral molecules to form negative ions. When an electric field is applied to the gas, the ions drift along the lines of force, thus producing an ionization current. Under usual conditions, electrons drift at speeds of the order of 10^6 cm/sec. The drift velocity of ions is many orders of magnitude less. Collisions with gas molecules prevent their attaining high velocities. Table 2.1–1. shows the average energy, W_{air}, expended in the production of an ion pair in air. As can be seen, this quantity does not depend markedly on the energy, and is approximately the same for electrons and alpha particles, when measured in the same gas (see also Valentine and Curran, 1958).

For details of the ionization process see Wilkinson [1950] and Price [1958].

TABLE 2.1–1. *Average energy expended in the production of an ion pair in air*

Radiation	W_{air} in electron volts per ion pair	Reference
$H^3\beta$	33.9	Jesse and Sadauskis, 1955.
$S^{35}\beta$	33.7	Bay, Mann, Seliger, and Wyckoff, 1957.
$S^{35}\beta$	33.6	Gross, Wingate, and Failla, 1957.
$Ni^{63}\beta$	34.0	Jesse and Sadauskis, 1955.
2-Mev X rays	33.9	Weiss and Bernstein, 1955.
$Po^{210}\alpha$	35.5	Jesse and Sadauskis, 1953.
$Po^{210}\alpha$	35.0	Bortner and Hurst, 1954.

2.1.1. *The current ionization chamber.* When an ionization chamber is in a radiation field, the measured ionization current first increases with increasing voltage and then levels off. Figure 2.1–1. shows the so-called "saturation" curve. In general, the voltage required to attain saturation current for any chamber will depend on the rate at which ionization is being produced. At saturation, the average ionization current, I, is related to the number of ion pairs produced per unit time, N, by the equation

$$I=Ne, \tag{1}$$

where e is the electronic charge. The chamber therefore measures the integrated effect of a large number of ionizing events. The time constant of the current-detecting device is generally made long to suppress statistical fluctuations, and whether the electrons are collected as free electrons (as for instance in argon), or attached to slow-moving molecules as

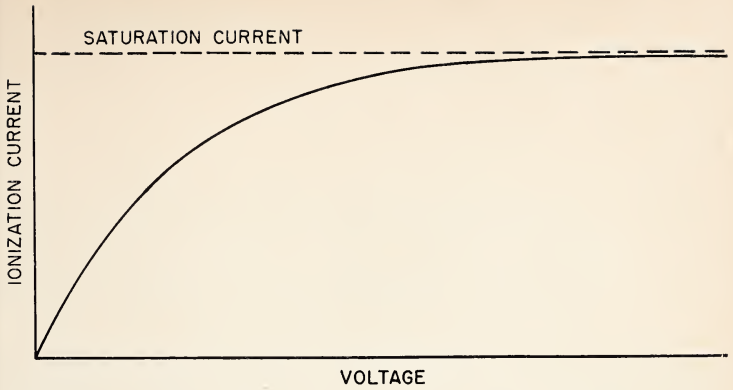


FIGURE 2.1–1. *Saturation curve (ion current versus collecting voltage) for a typical ionization chamber.*

ions (as for instance in oxygen), is of no importance. However the probability of recombination is lower in a gas in which free electrons only are formed, and saturation can be reached with a lower field strength.

When the ionization current is sufficiently large it can be measured with a microammeter. Generally, however, it is necessary to use more sensitive methods, for instance by allowing the charge to collect on a capacitor and measuring rate of change of voltage with an electrometer.

This ionization current depends on the mass of gas in the chamber, and therefore, in unsealed chambers, corrections for temperature and pressure must be made.

2.1.2. *Pulse ionization chamber.* With a fast amplifier the total ionization of a single heavily ionizing individual particle (or a group of simultaneous particles) passing through the sensitive volume can be measured. Suppose that the chamber is filled with gas in which free electrons are formed. If the voltage drop due to the ionization current is measured across a high megohm resistor, R, and the capacity of the electrode and measuring system is C, a voltage-time dependence is found, such as is shown in the lower curve of figure 2.1–2 (drawn for $RC=1$ μsec). When the time constant is increased, the voltage rises as shown in the upper curve ($RC=\infty$) of figure 2.1–2. Here, a fast rise (to point A) at the beginning of the pulse, due to the rapidly moving electrons, is followed by a slower increase (to point B) due to the movement of the positive ions. When it is feasible to use a gas which allows electron

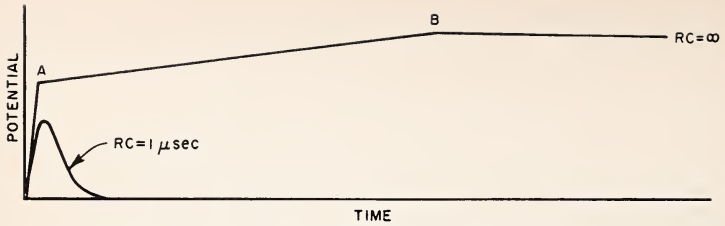


FIGURE 2.1–2. *Voltage pulse on collecting electrode of pulse ionization chamber.*
[Halliday, 1955; courtesy of John Wiley and Sons.]

collection, a time constant (RC clipping) of only a few microseconds is usually chosen to prevent pulse pile-up at high counting rates. If the clipping time is longer than the time for electron collection but much shorter than for collection of the positive ions, the pulse shape is determined by the movement of the electrons. The remaining positive ions induce a charge in the electron-collecting electrode and reduce the pulse amplitude, the magnitude of this charge depending on the location of the initial ionization. Therefore, in a parallel-plate chamber, the pulse amplitude will depend on where the ionizing particle traversed the chamber. This undesirable effect can be overcome by placing a grid in the chamber (e.g., Frisch grid chamber) to screen the collecting electrode from the positive ions. The induced charges from the positive ions can also be reduced by using a wire as the collecting electrode, usually in a cylindrical ionization chamber.

The use of a fast ionization chamber is limited at low particle energies by the inherent noise of the associated amplifier. This noise is equivalent to the arrival on the ionization-chamber anode of about 2000 electrons, which might represent an energy of about 70,000 ev dissipated by a particle traversing the chamber. For details see, for instance, Price [1958].

2.2. Proportional Counters

When the electric field strength at the center electrode of a fast ionization chamber is increased above a certain level, the size of the output pulse from the chamber starts to increase but is still proportional to the initial ionization. A device which is operated in such a fashion is called a proportional counter. The great advantage of the proportional counter is that it allows one to detect a very low initial ionization, even down to a single ion pair.

For a counter with cylindrical geometry, the field strength, E_r, at radius r is given by

$$E_r = \frac{V_0}{r \ln b/a}, \tag{1}$$

where a is the radius of the inner cylinder, which is usually a wire, b is the radius of the outer cylinder, and V_0 is the voltage applied to the counter. The field strength close to the wire increases rapidly and the electrons drifting toward the wire acquire enough energy between collisions to produce secondary ions and electrons; the latter are accelerated and produce more secondary electrons. Thus an avalanche is developed. However, photons are also formed during the production of the secondary electrons. These photons may release photoelectrons anywhere in the counter volume or walls.

If each electron produced in the primary ionizing event forms a total of n secondary electrons by collision, and γ is the probability that a photoelectron is formed per secondary electron, the electron avalanche forms $n\gamma$ photoelectrons. One can assume that each photoelectron forms n electrons by collision; hence, there is a second avalanche of $n^2\gamma$ electrons which, in turn, forms further photoelectrons. The final number of electrons is

$$M = n + n^2\gamma + n^3\gamma^2 + \ldots, \tag{2}$$

where M is called the multiplication factor.

In a proportional counter $n\gamma$ is less than one and the series converges so that

$$M = \frac{n}{1 - n\gamma} \tag{3}$$

and the total number of secondary electrons is proportional to the number of primary ion pairs. This is the essential property of a proportional counter.

Multiplication factors have been worked out theoretically [Rose and Korff, 1941]. Figure 2.2–1. shows experimental values for M as a function of applied voltage for argon.

2.2.1. *Shape of the output pulse.* In contrast to the pulse ionization chamber where the main part of the pulse is determined by the rapid movement of electrons, the pulse shape measured on the wire of a proportional counter is essentially determined by the movement of the positive ions. Since, in a proportional counter most of the ionization develops very close to the wire, the electrons travel only

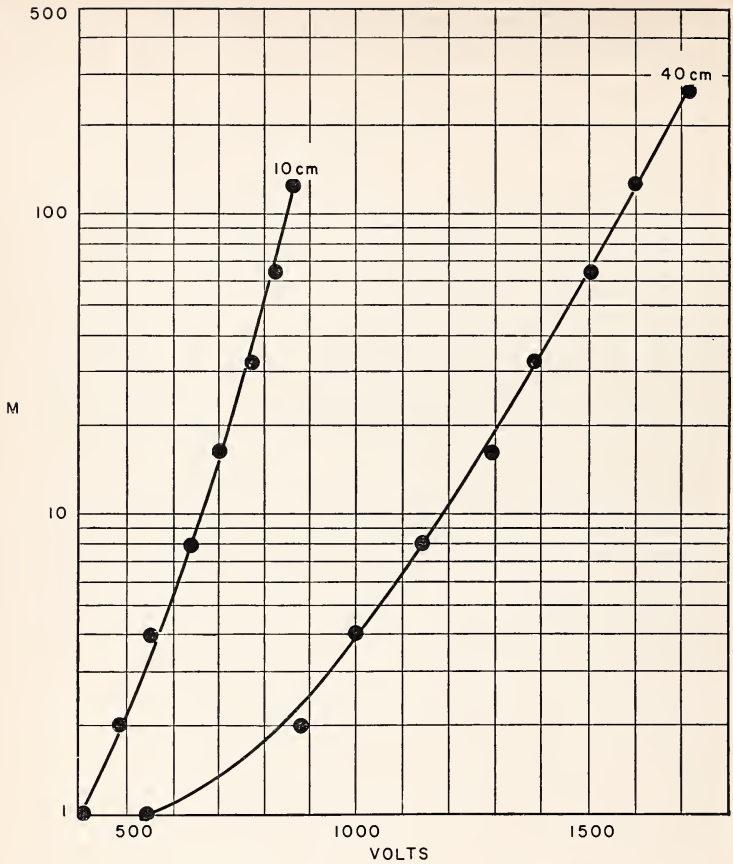


FIGURE 2.2–1. *Multiplication factor, M, as function of applied voltage for argon at pressures of 10 and 40 cm* Hg, *radius of center wire = 0.005 in., radius of outer electrode = 0.435 in.*

[Segré, 1953, pt. I, Detection methods, H. H. Staub; courtesy of John Wiley & Sons, New York, N.Y.]

short distances and their effect on the pulse rise is rather small. Figure 2.2–2. shows a typical pulse shape. A delay, of time t_1, elapses before the primary electrons reach the multiplication region. This time t_1 is determined by the location of the initial ionization in the counter and (depending on its construction) may be of the order of 1 μsec. This delay time, which is variable, should not be overlooked when coincidence experiments are carried out.

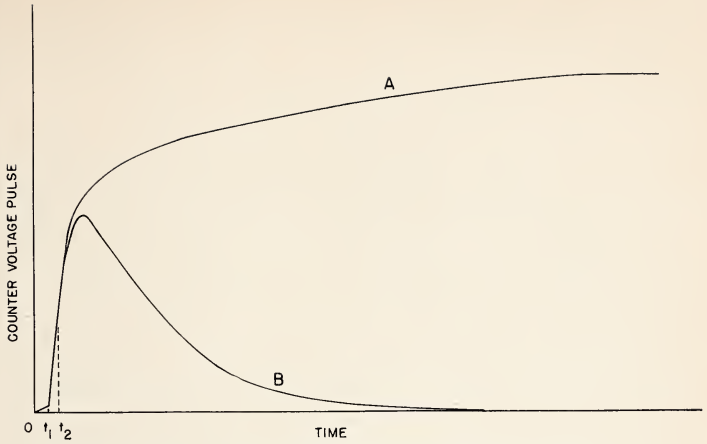


FIGURE 2.2–2. *Voltage pulse from proportional counter.*
Rossi, 1952; courtesy of Prentice-Hall.]

Initially the pulse rises very fast (curve A), first mainly as a result of the movement of the electrons (t_1 to t_2), then of the positive ions traveling in the strong field near the wire. As the positive ions move into the region of weaker field, the rise is slower and ceases when the ions reach the outer cylinder. This, for an average counter, takes about 200 μsec.

Curve A shows the shape of the voltage pulse for no loss of charge from the anode wire (i.e., for an infinitely long time constant). In practice, in order to improve the time resolution, a suitable clipping-time constant (RC) is used in the output to give the type of pulse shown by curve B. Clipping times as short as 0.1 μsec have been used. The chief criterion here is to keep the amplitude of the pulse, which is decreased by clipping, sufficiently large to overcome the amplifier noise level.

Since all the pulses will have the same general shape (except when the ionizing event takes place very close to the wire), the height of the clipped pulse will be proportional to the initial ionization. However, ionization and the formation of the electron cascade are statistical processes and a distribution in the height of the output pulses is observed, which broadens when the initial ionization decreases. [For further details, see Rossi, 1952, and Wilkinson, 1950.] A further spread can also be caused by a nonuniform center wire and by end-effects, both of which cause varying field distributions along the wire. However, in most cases the

shape of the outer electrode is unimportant. Since the avalanche takes place very close to the wire and it is only necessary to have saturation for ion collection through the whole of the sensitive volume, proportional counters can be built having variously shaped outer electrodes.

2.2.2. *Choice of counting gas.* A proportional counter should be filled with a gas in which the negative charge is carried by electrons. However, some such gases such as hydrogen, nitrogen and the noble gases exhibit a rapid change of multiplication factor, M, with applied voltage due to the appearance of photoelectrons. Complex molecules which absorb photons give better stability. Methane or methane-argon mixtures are in common use and multiplication factors up to 10^5 are possible.

2.2.3. *Applications of proportional counters.* The proportional counter can be used to determine the energy of particles and photons if they are totally absorbed in the counting gas. For low-energy X and gamma radiation, almost complete absorption can be achieved with a suitable gas filling (fig. 2.2–3).

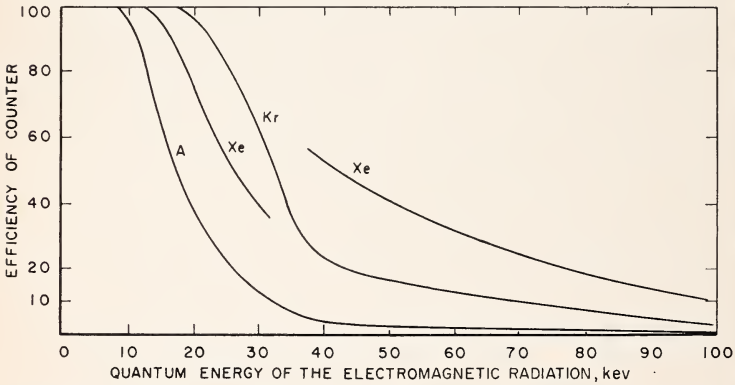


FIGURE 2.2–3. *Percentage of quanta absorbed in 50 mg/cm² of argon, krypton, and xenon (i.e., 5-cm path at 5 atmospheres in argon, at 2.5 atmospheres in krypton, or at 1.5 atmospheres in xenon).*
[Curran, 1950; courtesy of Atomic World, formerly Atomics.]

Proportional counters also have wide application to particle counting without energy discrimination. The source itself can be placed inside the counter, avoiding window absorption, and it is possible to work at atmospheric pressure, generally with methane or methane-argon mixtures, under a continuous gas flow (flow counter). Counter pulses due to a beta spectrum may vary in size by a factor of about

1,000, therefore the associated amplifier must have wide-range characteristics (see sec. 3.1). Excellent plateaus (counting rate versus applied voltage, or with varying discrimination at constant voltage) can be obtained.

2.3. Geiger-Müller Counters

If the voltage on a proportional counter is increased, $n\gamma$ becomes greater than one (sec. 2.2, eq (2)) and the series diverges. Under these conditions a discharge takes place, which spreads all along the wire forming an ion "sheath," and gives an output-pulse of several volts, independent of the initial ionization. Less additional amplification is therefore required than for proportional counters.

Unless the discharge is "quenched" it may be self-sustaining or multiple pulses may occur. Such quenching may be achieved externally, by electronic means, or internally by adding a suitable polyatomic gas. A gas filling which has been frequently used is argon at a pressure of about 9 cm Hg with ethyl alcohol vapor, or similar organic gas, at a pressure of about 1 cm Hg. The stabilizing action is believed to be due to the following fact:

Alcohol has a lower ionization potential than argon, so that the ions moving towards the cathode will, after a few collisions, consist only of alcohol ions. In contrast to argon ions, alcohol ions do not produce secondaries when being neutralized at the cathode. Therefore multiple pulsing is avoided. However, the alcohol ions dissociate upon being neutralized and when the supply of alcohol is exhausted, after about 10^8 counts, poor plateau characteristics result. Halogen vapors also have the same quenching effect [Liebson and Friedman, 1948; Friedman, 1949]. Since the halogen ions do not dissociate, the counter has a practically indefinite life. The operating voltage is also considerably lowered. Argon, with the addition of small quantities of xenon, nitrogen, and oxygen, has also been found to be a satisfactory filling for Geiger-Müller counters [Shore, 1949; Collinson, Demetsopoullos, Dennis, and Zarzycki, 1960].

After an ionizing event, the sheath of ions along the counter wire effectively lowers the wire potential and makes the counter inoperative until the ions have drifted to the cathode. Dead times therefore are long, of the order of 300 μsec, and thus the Geiger-Müller counter does not allow of such high counting rates as the proportional counter. It is also inferior because the slopes of the Geiger-Müller-counter plateaus are steeper than those of proportional

counters, values of less than 1 percent variation in counting rate per hundred volts being uncommon unless an artificial dead time is used to reduce spurious counts. When it is necessary to establish an absolute counting rate, it is difficult to know which point of the plateau corresponds to the true counting rate. This is not so serious with a proportional counter where a plateau slope as low as 0.1-percent counting-rate change per hundred volts can be achieved. Therefore, for standardization work, or for any other precise counting, preference should be given to the proportional counter. Length-compensated counters, for internal counting of radioactive nuclides in the gaseous form, give relatively flat differential plateaus in both the Geiger-Müller and proportional regions (sec. 3.3).

2.4. Scintillation Counters

It has been long known that many substances emit visible light when exposed to nuclear radiations, and this property has been employed as the basis for the detection of these radiations. The operation of a scintillation detector can be divided into the following distinct and consecutive stages:

2.4.1. *The absorption of the primary radiation.* A charged particle incident on the scintillator may dissipate all its energy within the scintillator provided that the dimensions of the scintillator are greater than the range of the particle. When gamma radiation is incident, there are three principal processes which result in the production of charged particles whose energy may be absorbed; namely, the Compton effect, the photoelectric effect, and pair production. The mass absorption coefficients for total absorption (attenuation) and true (energy)[1] absorption for these processes in sodium iodide are shown in figure 2.4–1. as a function of gamma-ray energy, while similar quantities for anthracene are given in figure 2.4–2.

The photoelectric and pair-production processes result in a well-defined energy release, as opposed to the continuous distribution observed in the Compton process, and hence discrete lines are obtained in the pulse-height spectrum. Some typical distributions obtained with monoenergetic gamma rays incident on a sodium iodide (thallium-activated) crystal, are shown in figures 2.4–3. to 2.4–6.

---

[1] In considering energy conversion in a small mass, one must also remember that in the photoelectric effect and in pair production, energy may escape in the form of characteristic X rays and annihilation quanta.

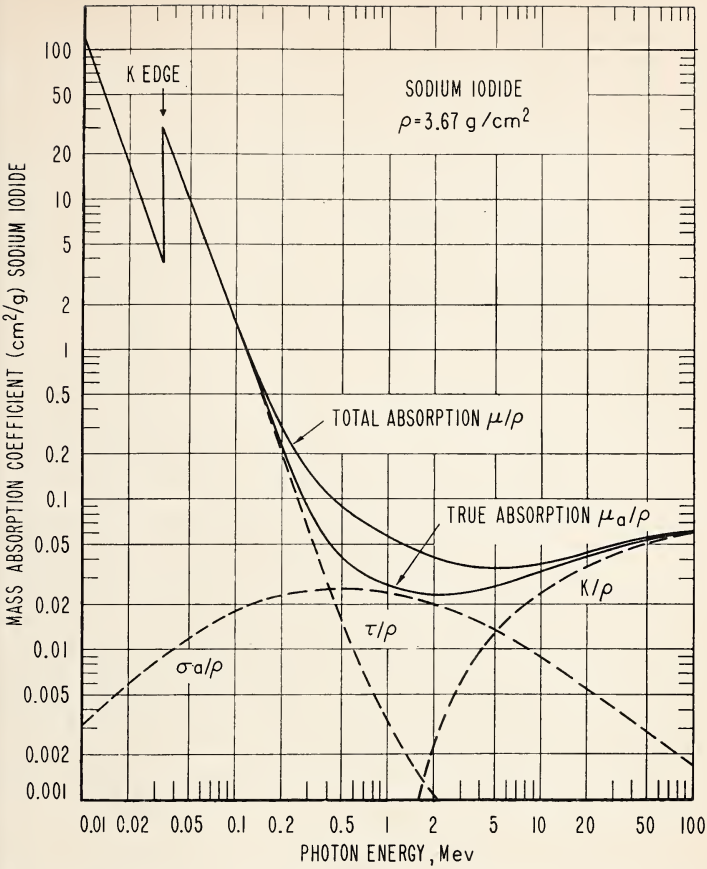


FIGURE 2.4–1. *The γ-ray mass-absorption coefficients of sodium iodide* versus *γ-ray energy.*

[Hine and Brownell, 1956, ch. 6, Scintillation detectors, W. J. Ramm; courtesy of Academic Press.]

2.4.2. *The conversion of the absorbed energy into photons.* A small portion of the energy dissipated by a charged particle in a scintillating medium is emitted as photons of visible and ultraviolet light. The number of photons, of average energy $h\nu$, produced by the absorption of energy E within the scintillator may be written:

$$p = \frac{E}{h\nu}\,\epsilon_p. \tag{1}$$

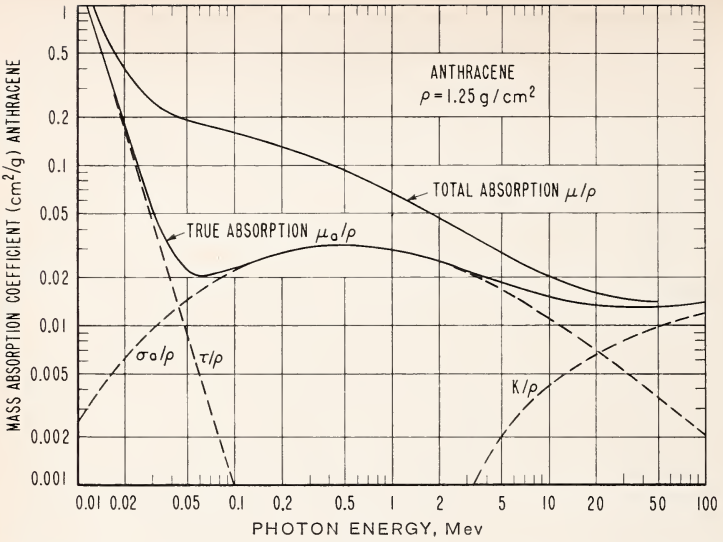


FIGURE 2.4–2. *The γ-ray mass-absorption coefficients of anthracene versus γ-ray energy.*

[Hine and Brownell, 1956, ch. 6, Scintillation detectors, W. J. Ramm; courtesy of Academic Press.]

The quantity ϵ_D is often referred to as the intrinsic efficiency of the scintillator. It is independent of energy for particles of low specific ionization; however for certain scintillators, notably the organic ones, the intrinsic efficiency decreases with increased specific ionization.

The time dependence of photon emission appears to follow an exponential law of the type

$$p(t) = \text{const}\ (1 - e^{-t/\tau}) \tag{2}$$

where $p(t)$ is the total number of photons emitted during the time t. The decay time τ is a characteristic of the scintillating material and essentially determines the maximum rise-time of the pulses that can be obtained from the material. In some materials, weak light emission may continue for times which are several orders of magnitude longer than the main decay time [Harrison, 1954].

2.4.3. *The attenuation of the emitted photons and their detection.* Of the photons produced in the scintillator, the number detected depends on the geometry and the optical properties of the system, including those of reflectors and any light guides between the scintillator and the cathode of the

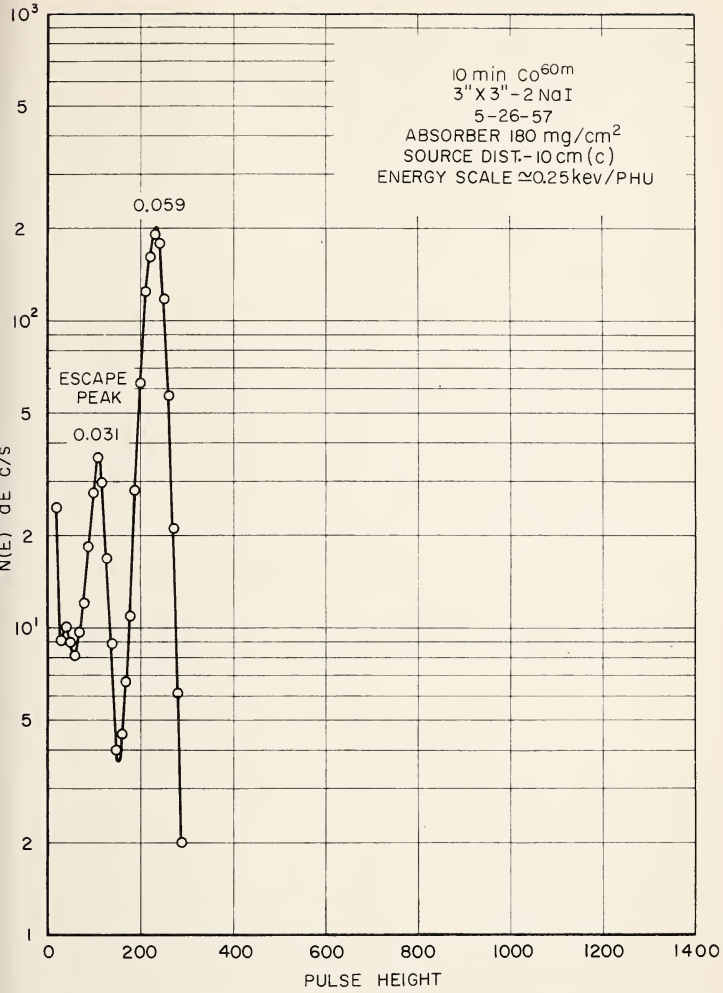


FIGURE 2.4–3. *Pulse-height distributions for 0.059-Mev gamma rays incident on a thallium-activated sodium iodide crystal.*
[Heath, 1957; courtesy of U.S. Atomic Energy Commission.]

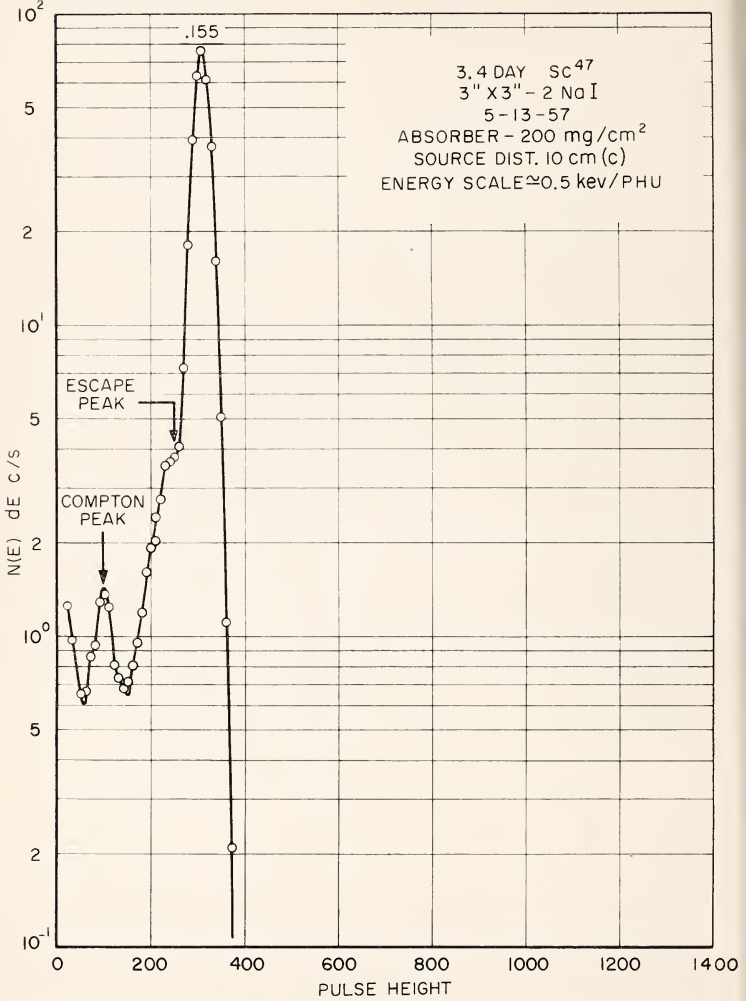


FIGURE 2.4–4. *Pulse-height distributions for 0.155-Mev gamma rays incident on a thallium-activated sodium iodide crystal.*
[Heath, 1957; courtesy of the U.S. Atomic Energy Commission.]

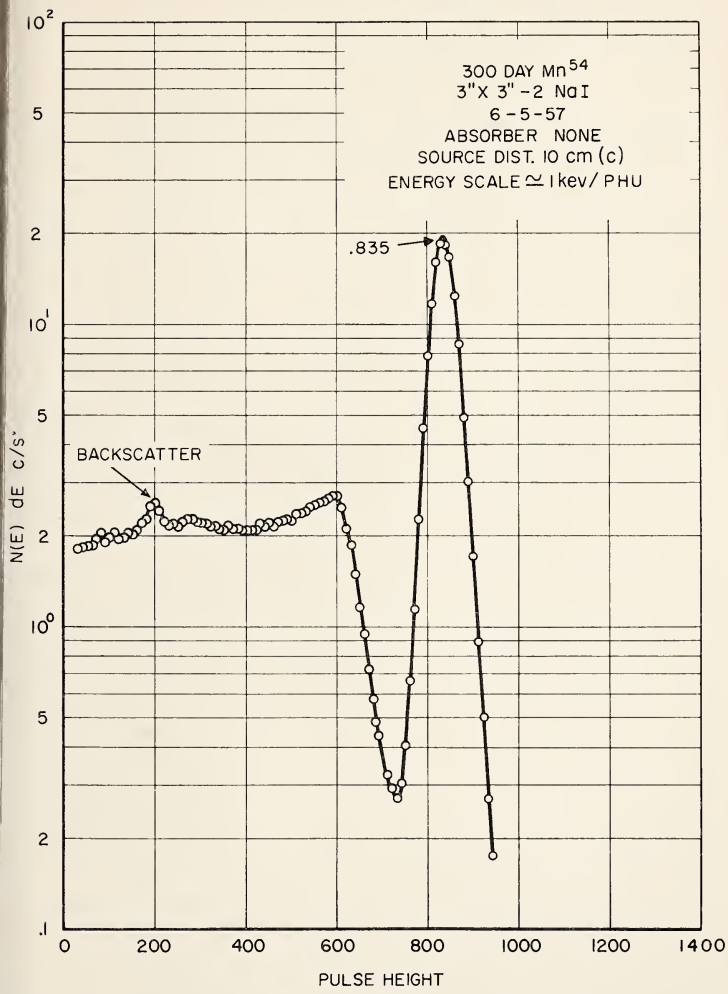


FIGURE 2.4–5. *Pulse-height distributions for 0.835-Mev gamma rays incident on a thallium-activated sodium iodide crystal.*
[Heath, 1957; courtesy of U.S. Atomic Energy Commission.]

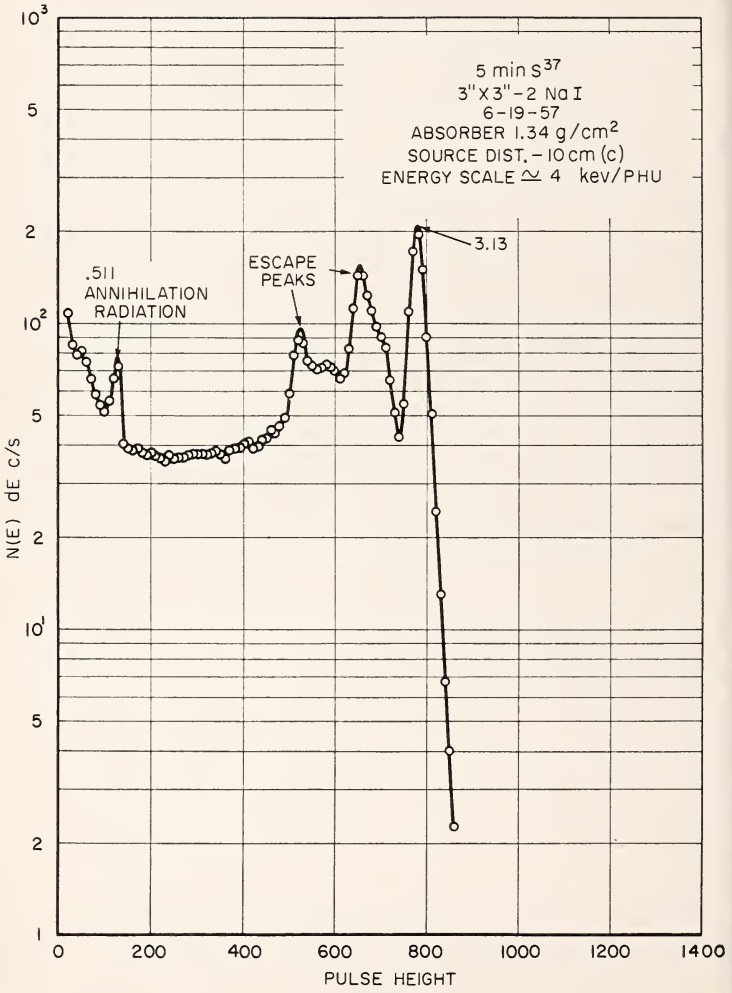


FIGURE 2.4–6. *Pulse-height distributions for 3.13-Mev gamma rays incident on a thallium-activated sodium iodide crystal.*
[Heath, 1957; courtesy of U.S. Atomic Energy Commission.]

electron-multiplier phototube that is used for detection. For good scintillators and reasonable geometries, these factors, ϵ_L, can, in general, be kept high. The photons falling on the cathode surface of the phototube are converted into electrons with an efficiency ϵ_C. Thus, the number of photoelectrons produced by p initial photons is

$$P=\epsilon_L \epsilon_C p. \tag{3}$$

Typically, ϵ_L may be as large as 50 percent while ϵ_C usually lies between 5 and 10 percent. In order to make ϵ_C as large as possible, the phototube should be so chosen that its spectral response curve closely matches the photon spectrum of the scintillator. Combining eqs (1) and (3), the number of photoelectrons obtained for a given energy release E in the scintillator is given by

$$P=\frac{\epsilon_p \epsilon_L \epsilon_C}{h\nu} E. \tag{4}$$

The quantity $\frac{h\nu}{\epsilon_p \epsilon_L \epsilon_C}$ is sometimes used as a quality criterion of the detector and, under good conditions, has a value between 500 and 2,000 ev per photoelectron. This may be compared with the 25 to 40 ev required to produce one ion pair in a gas counter.

2.4.4. *The electron-multiplication process.* The photoelectrons ejected from the cathode of a phototube are accelerated towards the first dynode under the influence of the electric field. The dynode surface has the property of emitting secondary electrons (the number emitted is a function of the accelerating potential and, in practice, lies between 3 and 5) when struck by the incident particle. These secondary electrons are then accelerated toward a further dynode and the process is repeated. With 10 or more such stages, an overall gain up to 10^7 or 10^8 can be readily achieved.

2.4.5. *Characteristics of scintillation counters.* The relevant characteristics of some of the more commonly used scintillators are given in tables 2.4–1, 2.4–2, and 2.4–3.

Of the inorganic scintillators, the most widely used is the thallium-activated sodium iodide crystal. This material is highly transparent to its own radiation and can therefore be used in large thicknesses. This property, together with its high density, make it particularly suitable for measurements of gamma-ray spectra. Each gamma-ray line can give rise to several peaks in the pulse-height distribution so that complex gamma-ray spectra are sometimes difficult to inter-

TABLE 2.4–1. *Organic scintillators*

Scintillator	Density, g/cm³	Effective atomic number, $\bar{Z}_\tau$	Wavelength of emission, A	Refractive index	Light yield	Decay time, 10^{-9} sec	Remarks
Anthracene	1.25	5.8	4,450		1.00	25	Large crystals not quite clear.
Quaterphenyl		5.8	4,380		0.85	8	Pure crystals difficult to synthesize.
Stilbene	1.16	5.7	4,100		.73	7	Good crystals readily obtainable.
Diphenyloxazole		6.1			.78		
Diphenylbutadiene.		5.7	4,610		.67	8	
Diphenylanthracene.		5.8	4,800		.65		
Terphenyl (para)	1.23	5.8	4,150		.55	12	Good crystals readily obtainable.
Diphenylacetylene		5.8	3,900		0.26–0.92	7	
Phenanthrene	1.03	5.8	4,350	1.66	.46	10	Clear crystals difficult to obtain.
Naphthalene	1.15	5.8	3,450	1.58	.15	75	Good crystals easy to obtain.
Chloroanthracene		9.8			.03		

TABLE 2.4–2. *Inorganic scintillators*

Scintillator (activator in parentheses)	Density, g/cm³	Effective atomic number, $\bar{Z}_\tau$	Wavelength of emission, A	Refractive index	Light yield (anthracene =1.00)	Decay time, μsec	Remarks
ZnS (Ag)	4.1	27	4,500	2.4	*(2.0)	*(>1)	Only very small crystals, transparency poor.
CdS (Ag)	4.8	44	7,600	2.5	*(2.0)	*(>1)	Only small crystals, yellow.
NaI (Tl)	3.67	50	4,100	1.7	2.0	0.25	Excellent crystals available, hygroscopic.
KI (Tl)	3.13	49	4,100	1.68	0.8	>1	Excellent crystals available, not hygroscopic.
NaCl (Ag)	2.17	16	2,450, 3,850.	1.54	1.15	>1	Excellent crystals available.
LiI (Tl, Sn, or Eu).	4.06	52	Blue-green.	1.95			Activation problems, hygroscopic.
LiF (AgCl)		8.1		1.39	0.05		
CsI (Tl)	4.51	54	White	1.79	1.5	>1	Excellent crystals obtainable, not hygroscopic.
CsBr (Tl)	4.44	49		1.70	2.0	>1	
$CaWO_4$	6.06	59	4,300	1.92	1.0	>1	Small crystals, transparency good.

*The light yield and the decay time of the zinc-sulfide and cadmium-sulfide phosphors depend strongly on former treatment (quenching) and intensity of excitation. To a lesser degree this is also the case for other inorganic phosphors.

TABLE 2.4–3. *Liquid and plastic scintillators*

Scintillating solute	Solvent	Optimum concentration g/liter	Density, g/cm³	Effective atomic number, $\bar{Z}_\tau$	Wavelength of emission, A	Refractive index	Light yield (anthracene =1.00)	Decay time*, 10^{-9} sec
	Xylene	5	0.87	5.6	3,700	1.50	0.48	7
p-Terphenyl	Phenylcyclohexane.	3	.94	5.6	3,700	-------	.48	8
2,5-Diphenyoxazole (PPO).	Xylene	5	.87	5.6	3,800	1.50	.46	6
Naphthylphenyloxazole (α-NPO).	Xylene	4	.87	5.6	3,600	1.50	.40	7
9,10-Diphenylanthracene.	Phenylcyclohexane.	5	.94	5.6	4,800	-------	.39	12
Phenyl α-naphthylamine.	Phenylcyclohexane.	3.5	.94	5.6	3,800	-------	.37	-------
Diphenylhexatriene.	Phenylcyclohexane.	1.6	.94	5.6	4,600	-------	.21	10
Terphenyl	Polystyrene	†31	1.06	5.7	-------	1.59	.30	(5)
4% Terphenyl +0.2% diphenylstilbene.	Polyvinyltoluene.	†40	-------	-------	-------	-------	.54	-------
Tetraphenylbutadiene.	Polystyrene	†17	1.06	5.7	-------	1.59	.37	(5)

*Decay times measured with fast oscilloscopes. No correction for the uncertain phototube transit times has been made. Corrected decay time or decay times found by fluoroscopic methods with ultraviolet light seem to lie in the vicinity of 3×10^{-9} sec for many liquid and plastic scintillators.

†Grams of solute per 1,000 g of solvent.

pret. Besides the full energy peak associated with total energy dissipation of each gamma-ray line, there may be other peaks together with a broad Compton distribution present in the spectrum (see figs. 2.4–3, 2.4–4, 2.4–5, and 2.4–6). A discussion of the distributions shown in these figures is given by Heath (1957). An important consideration in the analysis of spectra is the resolution, or width at half height, of the full energy peak. The finite resolution arises from the variance in the number of photoelectrons produced at the cathode of the phototube and from the statistical nature of the electron-multiplication process, and therefore varies with energy. Under the best conditions presently available this may be perhaps 6 to 7 percent for the 662-kev radiation of barium-137.

Owing to the low average atomic number of organic scintillators, the photoelectric and pair-production cross sections are greatly reduced and hence such materials lend themselves primarily to the detection of charged particles and also neutrons, which produce proton recoils in the usually hydrogeneous material of the scintillator. Some range-energy curves for ionizing particles in anthracene are given in figure 2.4–7.

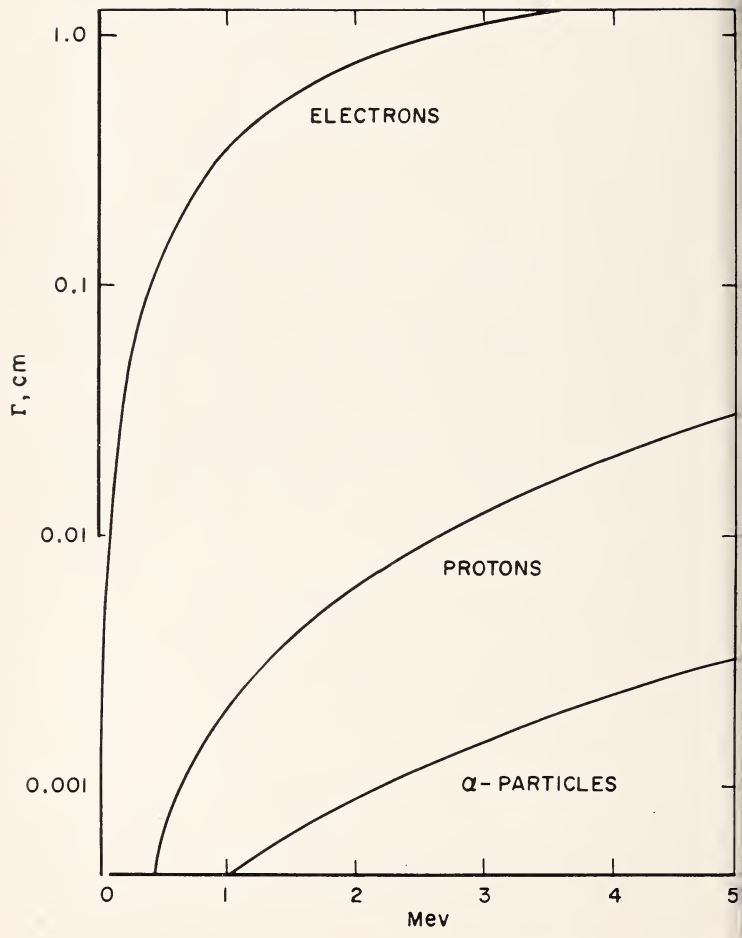


FIGURE 2.4–7. *Range-energy curves for ionizing particles in anthracene.* [Birks, 1953; courtesy of McGraw-Hill.]

2.5.1. *Statistics of pulse counting.* The process of radioactive decay is a random phenomenon; the events being counted form a random sequence in time. Therefore counting for a finite period of time can only yield an estimate r of the true, average counting rate $\bar{r}$. The measured r is subject to statistical fluctuations. The probability that a certain number of events n occurs within a time t can, however, be expressed mathematically by the Poisson and Gauss distributions.

From these, an expression for the error of a measurement can be derived; this is the standard deviation. For large n, the standard deviation in the total count is

$$\sigma=\sqrt{n}. \tag{1}$$

The standard deviation in the counting rate is

$$\sigma_r=\frac{1}{t}\sqrt{n}=\sqrt{\frac{r}{t}}. \tag{2}$$

The standard deviation is a measure of the scatter of a set of observations around their mean value. For example, about 10,000 counts are necessary for a standard deviation in the total count of ± 100 or of ± 1 percent. The probability of a single observation being within the standard deviation from the mean is 0.68. In other words, when many observations are made, approximately two-thirds of the observations ought to lie within the standard deviation from the mean and the remainder outside. This fact allows an appraisal of the performance of a counting system to be quickly made.

Since radioactive decay is a statistical process, one should be equally suspicious when the set of observations appears considerably more precise than predicted as when it is considerably less precise. A rigorous evaluation of counter performance may be obtained from the "chi-square" test [Fisher, 1950].

In the presentation of data, the standard deviation is usually given to indicate the precision of measurement. The following confidence limits apply to representative multiples of the standard deviation:

Deviation	$\pm 0.675\sigma$	$\pm\sigma$	$\pm 2\sigma$	$\pm 3\sigma$.
Probability that observation lies within this deviation	0.5	0.68	0.95	0.997.

The deviation equal to $\pm 0.675\sigma$ is called the "probable error" of an observation. There is a 50-percent chance that another observation will lie within these limits.

The above data allow one to estimate if a counting rate deviates by more than the statistical fluctuations from a previously determined rate. This is of importance when equipment is checked routinely with a performance standard (see sec. 1.1). For instance, a deviation of more than 2σ from a previously established mean should be considered with suspicion since the probability of this occurring is only 5 percent. (For further details, see Evans, 1955, ch. 27; and Quimby, Feitelberg, and Silver, 1958, pp. 179 to 182.)

2.5.2. *Background considerations.* In most instances the radiation counter exhibits a background rate which is not negligible and which has to be subtracted from the gross counting rate. The statistical fluctuations of the background must be included in the estimate of the error. According to the theory of errors the standard deviation of the net counting rate is

$$\sigma=\sqrt{\sigma_{\mathrm{T}}^2+\sigma_{\mathrm{B}}^2}=\sqrt{\frac{r_{\mathrm{T}}}{t_{\mathrm{T}}}+\frac{r_{\mathrm{B}}}{t_{\mathrm{B}}}}. \tag{3}$$

T refers to the total counts and B to the background. In counting sources of reasonable activity, it is usually sufficient to determine the background counting rate only once (or perhaps before and after a series of samples) by counting long enough to make σ_{B} negligible compared to σ_{T}. The optimum division of available time between background and source counting is given by

$$\frac{t_{\mathrm{B}}}{t_{\mathrm{T}}}=\sqrt{\frac{r_{\mathrm{B}}}{r_{\mathrm{T}}}}. \tag{4}$$

Here r_{B} and r_{T} have to be obtained from a preliminary run.

The minimum combined time necessary in order to achieve a predetermined precision can be estimated for particular values of total counting rate relative to background counting rate. Curves published by Loevinger and Berman [1951] enable this to be accomplished for any practical case. These curves are reproduced in figure 2.5–1. As an example of the application of these curves, suppose that it is desired to determine with a precision of ± 5 percent the activity of a sample which has a counting rate approximately half that of the background. Then k, the ratio of total to background counting rate, is 1.5, and from figure 2.5–1, the 5-percent line inter-

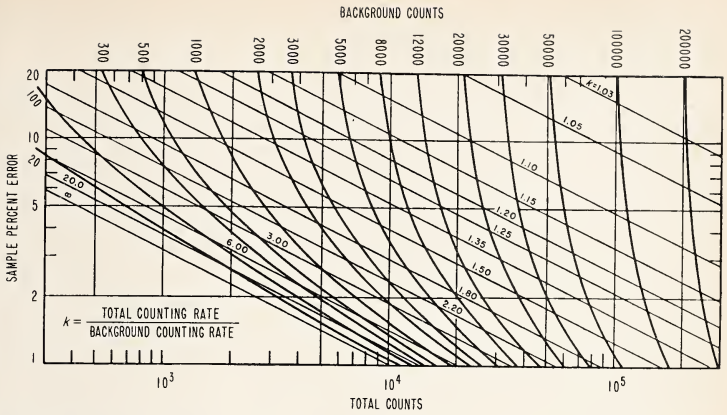


FIGURE 2.5–1. *Relationship between precision and number of observed counts taking account of background.*

For a given desired percentage error in the measurement of sample activity, the optimum distribution of counts between background and the combined background plus sample counts can be chosen so that the time spent in counting is a minimum. The curves are particularly useful when a predetermined precision is required in counting a sample of low counting rate using the pre-set count technique. [Loevinger and Berman 1951; courtesy of McGraw-Hill.]

sects the oblique line for $k=1.5$ at a total count of 6,600. The point of intersection lies about one-third of the distance between the background-count curves for 3,000 and 5,000. Thus, the background count should be about 3,600. These curves are very valuable whenever the preset-count technique can be used. A preliminary rough determination of the background and the total counting rates is necessary in order to establish the value of k. The preset-count technique used with these curves then enables all sample activities to be determined with the same precision.

2.5.3. *Minimum detectable activity.* Counting intervals cannot be made indefinitely long, therefore background considerations determine the minimum detectable activity. A good rule of thumb in this connection is the following. Consider a count which is different from the background count by little more than the standard deviation of the background fluctuations. Such a count suggests that an effect has been observed but does not establish it. If the count is different from the background count by more than twice the standard deviation of the background count one can believe, with reservations, that an effect has been observed. Only if the effect is such that the count is different from the background count by more than three times the standard deviation of the background count can it be considered as established, since

the probability of its being due to background fluctuations alone is then only 0.3 percent. (See table in sec. 2.5–1.) [De Benedetti and Findley, 1958].

The *minimum detectable activity* can therefore, on this basis, be considered to be that amount of activity which, in the same counting time, gives a count which is different from the background count by three times the standard deviation of the background count.

2.5.4. *Background equivalent activity.* A useful concept for expressing the intrinsic sensitivity of any detector is that of the Background Equivalent Activity (BEA) [Seliger and Schwebel, 1954; Mann and Seliger, 1958a, table 3]. This quantity, for any given instrument and radioactive nuclide, is, as its name implies, the activity of that nuclide which will, in the particular geometry used, produce a response of that instrument which is equal to its background reading. The minimum detectable activity with regard to any radionuclide and measuring system will be a fraction of the background equivalent activity.

2.5.5. *Counting losses.* After detection of a pulse the counter and the associated electronic equipment are inoperative for a short interval (the "dead" time τ) causing a certain fraction of counts to be lost. A complete treatment on counting losses has been given, amongst others, by Elmore [1950]. For a nonextendable dead time, τ, the true counting rate, R, is given by

$$R=\frac{r}{1-r\tau} \tag{5}$$

where r is the observed counting rate. Dead times for Geiger-Müller counters can be from 100 to 300 μsec. Dead times for proportional and scintillation counters depend essentially on the associated electronic circuitry and are usually of the order of a few microseconds. Counting rates where the losses exceed 10 percent should be avoided.

The following are some of the methods available for determining the dead time:

(a) *Half-life measurement.* The activity of a radionuclide of relatively short half-life, for instance iodine-128, $T_{1/2}$ =24.99 min, is followed. The decay is plotted on semilogarithmic graph paper and compared with a straight line drawn for $T_{1/2}$=24.99. Corrections can then be taken directly from the graph, and avoids any calculation.

(b) *The two-source method.* Two sources of about equal activity are counted individually and together. Care should be taken that the presence of one source does not

influence the counting rate due to the other source (scattering). An approximate expression for the dead time [see, for example, Price, 1958] is

$$\tau=\frac{r_1+r_2-r_{12}-r_B}{r_{12}^2-r_1^2-r_2^2}, \tag{6}$$

where the r's are the total counting rates and the subscripts refer to the two sources; r_B designates the background rate. Since (6) contains differences of large numbers, the individual counting rates have to be determined with high precision.

(c) *Measurement with an oscilloscope.* A very quick estimate of the resolving time can be made when a pulse-triggered oscilloscope is connected at a point between the amplifier and scaler. Using the equipment at a high counting rate, the minimum time between the two successive pulses can be read on the oscilloscope screen. The scaler must have a shorter dead time than the preceding part of the equipment, but this condition is nearly always fulfilled in practice.

2.5.6. *Statistics of ionization chambers.* Statistical variations in the number of particles produced in a radioactive-decay process is reflected in the variation of total charge released in an ionization chamber (or "mean-level" system; see Price, 1958). The total charge, Q, collected in a given time in the chamber will be equal to the product qn, where q is the average charge released per nuclear particle and n is the number of particles interacting within the chamber in that time. Therefore the standard deviation in Q will be q times as large as the standard deviation in n, or $\sigma_Q=q\sqrt{n}$. Substituting $Q=qn$ one obtains

$$\sigma_Q=\sqrt{qQ}. \tag{7}$$

This treatment neglects the fluctuations in the charge released by the individual nuclear particles. Price [1958] gives the treatment for rate-type ionization-chamber instruments.

3. Principal Methods for Absolute Standardization

3.1. Standardization by 4π Counting

Perhaps the most widely applicable method for the standardization of alpha- and beta-emitting nuclides is that of 4π counting. This method involves the use of as thin a film as possible for the source mount and this film is looked at on

both sides by two detectors each subtending a solid angle of essentially 2π steradians at the source. This section will be limited to gas counters as detectors.

Several designs of 4π counters have appeared in the literature, including spherical, cylindrical, and pillbox types [Hawkings, Merritt, and Craven, 1952; Smith, D. B., 1953 and 1954]. Representative examples of these are given in figures 3.1–1, 3.1–2, and 3.1–3.

Figure 3.1–1 shows the National Bureau of Standards spherical counter in which a source is placed on the center of a metallized collodion film supported on an annular aluminum foil which divides the counter in half. Two loops of 0.001-in.-diameter wire form the anodes. Methane or a mixture of argon and methane is used as a flow gas at atmospheric pressure. A cylindrical type of 4π counter designed by the Atomic Energy Research Establishment at Harwell, is shown in figure 3.1–2. This counter is operated in the Geiger-Müller region using a "one-shot" filling of 90 percent argon and 10 percent ethyl alcohol at 10 cm of Hg pressure. It is, therefore, necessary to pump out the counter thoroughly, or flush with argon, before filling, each time a source is inserted. A counter of this geometry could equally well be operated in the proportional region. Figure 3.1–3 shows a sketch of a simple pillbox type of counter which has been used by the Chalk River Laboratories. One desirable feature which is necessary for any counter which employs an internal source is that it should be readily demountable for decontamination should a source accidentally be dispersed inside the counter.

The intrinsic efficiency of a well designed 4π counter is assumed to be 100 percent for charged particles [Hawkings, Merritt, and Craven, 1952; Seliger and Schwebel, 1954]. Any departure from 100-percent efficiency that has been observed can be attributed to absorption by the source and the source mount. High efficiencies are also possible for X rays (electron-capturing nuclides) by operating at elevated pressures [Allen, 1957; Campion and Merritt, 1957].

Since the source mount forms an integral part of the counter cathode it must be sufficiently conducting to provide adequate field strength at the source and to prevent local charging. At the same time the mount must be as thin as practical to reduce absorption losses. A common technique is the use of a thin plastic film, which can be made as thin as 1 or 2 $\mu g/cm^2$ (see, for example, Pate and Yaffe, 1955a), and rendered conducting by the vacuum evaporation of a suitable metal onto the surface. Gold is commonly used since it is stable to most chemicals and can be readily evap-

FIGURE 3.1–1. *$4\pi\beta$ Proportional counter: spherical type.*
[Mann and Seliger, 1958a]

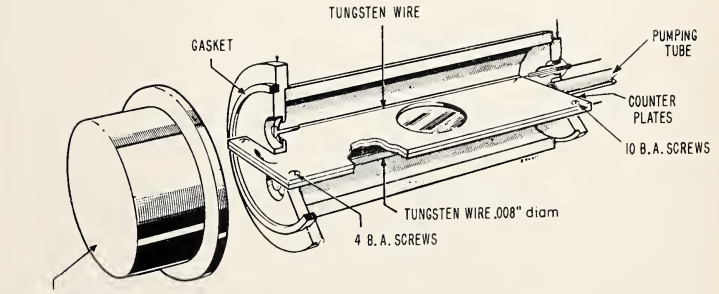


FIGURE 3.1–2. *$4\pi\beta$ Geiger-Müller counter.*
[Smith, D. B., 1953; courtesy of U.K. Atomic Energy Authority.]

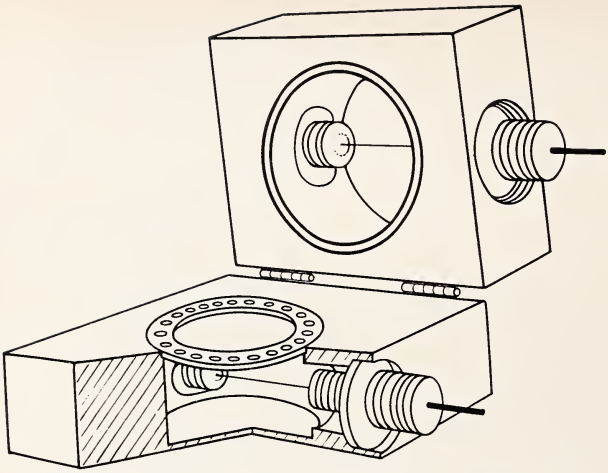


FIGURE 3.1–3. *$4\pi\beta$ Proportional counter: pillbox type.*

orated; other elements have been used. The amount of gold required to make a conducting surface is in some doubt, and apparently depends on the counter used; however, about 20 $\mu g/cm^2$ is probably sufficient for most cases. A simpler source mount can be made by depositing the source on a plastic film and then covering it with aluminum leaf ($\sim$200 $\mu g/cm^2$). This method results in a considerably thicker source mount and a correction must be made to allow for the absorption of the low-energy particles by the mount. These corrections have been discussed by Smith [1954], Hawkings, Merritt, and Craven [1952], Mann and Seliger [1953], and more recently by Pate and Yaffe [1955c].

The output pulse from proportional and some Geiger-Müller counters is such that external amplification is necessary. In the case of a proportional counter, the pulse height may vary over a considerable range, perhaps three orders of magnitude, and hence, good overload properties are required of the circuitry. The ideal characteristic of the external amplifier is a short dead time which is independent of input pulse height. This characteristic has been approached in recent amplifiers [Kelly, 1956; Fairstein, 1956]. If, however, there is a variable (extendable) dead time present anywhere in the counting system, this may be corrected by artificially introducing a constant paralysis time which is longer than any possibly occurring dead time. Such a technique is desirable when using Geiger-Müller counters, which have

variable dead times, and it also at the same time eliminates spurious counts. It should be noted that for absolute disintegration-rate determinations with, say, a $4\pi\beta$ proportional or Geiger-Müller counter, it is not necessary for the amplifier to be linear, since an indication of an event is all that is required.

The measurement of the activity of a source is normally made by plotting a curve of counting rate either against the potential applied to the counter, keeping the discriminator bias level constant, or against the discriminator bias for a fixed counter potential. (The first alternative must be used with Geiger-Müller counters.) The plateau may extend for some 200 volts of the applied potential and its slope determines the precision of the counting rate. The slope may be of the order of 0.1 percent per 100 volts. The counting rate so obtained must be treated for the following corrections:

3.1.1. *Dead time.* See section 2.5.

3.1.2. *Background.* This is readily obtained by inserting a blank source mount into the counter. The background rate is then subtracted from the observed counting rate after the correction for dead-time losses. The background rate in a well shielded proportional counter may be about 0.5 to 2 counts per second, but depends on the size. Part at least of the background is due to natural activity in the materials from which the counter is constructed, and a useful survey of the "cleanliness" of such materials is given by Grummitt, Brown, Cruikshank, and Fowler [1956]. However, the short dead times of proportional-counter systems allow such high counting rates that the background-rate correction is relatively very small.

3.1.3. *Source-mount absorption.* If necessary, a correction for the absorption in the source mount should be made. The analysis of Pate and Yaffe [1955b] is recommended for the most precise work.

For electron-capturing nuclides (X rays), difficulties arise because of uncertainties in the absorption of the soft Auger electrons. They are therefore filtered out by foils of suitable thickness. The fluorescence yield (fig. 3.1–4.) is then used to correct to the total disintegration rate. Theoretical or empirical corrections are also required for possible L and M capture.

3.1.4. *Self-absorption correction.* There is at present no general method for determining this correction with an accuracy comparable with that for other corrections in 4π counting. The technique of progressively diluting a stock solution until the observed activity expressed in terms of the original solution is a constant merely indicates that minimum

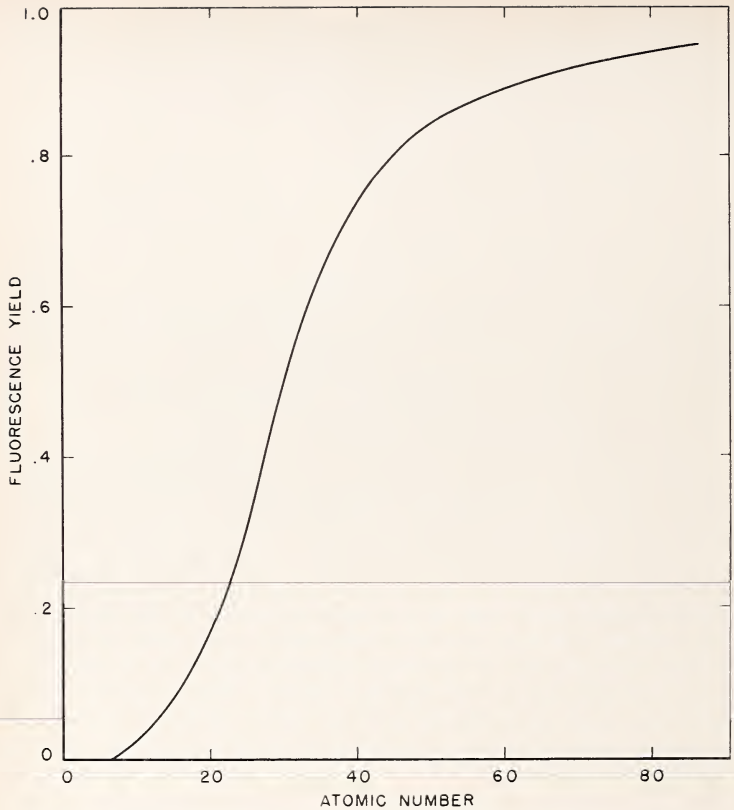


FIGURE 3.1–4. *Fluorescence yield as a function of atomic number.*
[See Condon and Odishaw, 1958, ch. 6 of pt. 9, Nuclear electromagnetic radiations, R. W. Hayward, pp. 9–115.]

self-absorption has been obtained rather than that the correction is zero. Calculated estimates based on the size of the crystals forming the active deposits and macroscopic absorption coefficients have been made by Meyer-Schützmeister and Vincent [1952] and Seliger and Schwebel [1954]. Yaffe and Fishman [1960] have used a vacuum-distillation method to set up self-absorption curves applicable to this source-preparation technique. Carswell and Milsted [1957] have used a spray technique to produce very thin sources but this technique does not permit of quantitative deposition. Recently Merritt, Taylor, and Campion [1959] have used the $4\pi\beta$-γ coincidence-counting technique to measure, under specified conditions, the self-absorption for a number of

radionuclides amenable to this technique. For a source of mean superficial density of $2\mu g/cm^2$ prepared by straightforward evaporation, the self-absorption varied between about 1.0 percent for sodium-24 (beta end-point energy 1.39 Mev) and 40 percent for the 86-kev beta transition in cesium-134. An appreciable improvement was found by using spreading agents (e.g., insulin as a wetting agent and colloidal silica as a seeding agent in the crystallization process), particularly for the weaker beta-emitters.

By incorporating into the same chemical compound two radionuclides, one a beta emitter and the other a previously standardized beta-gamma emitter, Merritt, Taylor, Merritt, and Campion [1960] (see also Campion, Taylor, and Merritt, 1960) have used $4\pi\beta$-γ coincidence counting to determine the self-absorption of sulfur-35.

3.1.5. *Decay.* When making a series of measurements on a short-lived radionuclide, the observations are usually corrected for decay to some reference time. If the period of time for which a count is taken is an appreciable fraction of the half-life, a correction for the decay during this period must also be made. It can be readily shown that the counting rate at the beginning of the count $N_{t=0}$ is given by

$$N_{t=0}=n_{\text{obs}}\frac{\lambda}{(1-e^{-\lambda t})} \tag{1}$$

where n_{obs} is the total number of counts observed during the counting period t and λ the decay constant.

3.1.6. *Standardization by 2π counting.* For the standardization of alpha-emitting nuclides it is possible to use a 2π geometry, which is essentially one-half of a 4π system. Although all of the considerations in 4π counting apply equally well here, certain characteristics of the alpha-particle-disintegration process allow this more restricted and simpler geometry to be used.

The source may be electrodeposited or evaporated onto a polished metal backing that behaves as a semi-infinite medium. Alpha particles, being more massive than electrons, are less easily backscattered from the backing so that the fraction of the alpha particles scattered into the forward direction is far less than in the case of beta particles. Also, alpha particles are emitted in monoenergetic groups with much higher energies than beta particles which are characteristically emitted in a spectrum of energies. The spread in voltage pulses from the 2π proportional counter will readily indicate the degree of source self-absorption present. When due regard is paid to the preparation of the source, which should be effectively "weightless" on a smooth backing, the

backscattering and source self-absorption effects can be made to be of the order of a few percent or less, while the corrections for these effects are of opposite arithmetical sign and tend to be self-canceling, so that the ultimate accuracy approaches that obtained by 4π counting.

3.2. Coincidence Counting

If a nuclide emits two or more simultaneous radiations, a measurement of its absolute disintegration rate may be made by the method of coincidence counting. Two detectors are required, each of which will respond, ideally, to one radiation only. In principle at least, it is not necessary to know the efficiency of either detector. For example, if we consider a radionuclide having a gamma ray following a beta transition, and having an absolute disintegration rate N, then, in principle*, the counting rates in the two counters and in the coincidence channel may be written:

$$\begin{aligned} N_\beta &= N_0\epsilon_\beta \\ N_\gamma &= N_0\epsilon_\gamma \\ N_c &= N_0\epsilon_\beta\epsilon_\gamma, \end{aligned} \tag{1}$$

where ϵ_β and ϵ_γ are the efficiencies (intrinsic detector efficiency *and* efficiency due to solid angle subtended by each detector to the source) of the beta and gamma detectors.

We thus obtain

$$N_0 = \frac{N_\beta N_\gamma}{N_c} \tag{2}$$

independent of the overall efficiency ϵ_β or ϵ_γ, of either counter.

Due to the spread in rise time of the pulses in the individual channels it is necessary to employ a coincidence mixer with a finite resolving time, τ_R, so that no true coincidences will be lost. As a consequence, not only will true coincidences be recorded in the coincidence channel, but also random events that occur within a time τ_R of one another. These random coincidences, often called accidental coincidences, are given, for low-efficiency detectors (Dunworth, 1940), by

$$N_a = 2\tau_R N_\beta N_\gamma. \tag{3}$$

*The relationships in the following paragraphs, and equations, have been discussed and derived in general terms and it must be understood that N_β, N_γ, and N_c are counting rates to which appropriate and small corrections, e.g., for background, should be made. Thus if N_β, N_γ, and N_c are *observed* counting rates, eq (2) is correct only *in principle* as corrections which are discussed later should be applied to it.

Using eq (3) to correct eq (2) for these random coincidences gives, neglecting second-order terms,

$$N_0 = \frac{N_\beta N_\gamma}{N_c}\left(1+2\tau_R \frac{N_\beta N_\gamma}{N_c}\right). \quad (4)$$

In practice some modifications to the above equations are necessary, as will be discussed below. The technique may be applied to β–γ [Dunworth, 1940], α–γ [Lyon and Reynolds, 1956], γ–γ [Hayward, Hoppes, and Mann, 1955], or γ–X-ray [Allen, 1957; Lyon and Reynolds, 1957] coincidence counting. Since the basic principle is the same for each of these, only β–γ and γ–γ coincidence counting will be described as typical examples.

As has been emphasized by Putman [1953], the coincidence method is valid with respect to extended sources provided that either detector is equally sensitive to all parts of the source.

3.2.1. *Beta-gamma coincidence counting.* The techniques applicable to β–γ coincidence counting using detectors whose efficiencies are relatively small have been described by several authors [Dunworth, 1940; Barnothy and Forro, 1951; Siegbahn, 1955, ch. 26 "Measurement of Disintegration Rate" by J. L. Putman; and Bay, 1956]. If, however, one detector approaches 100-percent efficiency, as, for example, by employing a 4π counter for the beta detector, the technique probably becomes one of the most powerful methods available at the present time for the standardization of those beta-emitting nuclides which may have a gamma ray in their decay scheme. A $4\pi\beta$–γ coincidence unit employing a liquid scintillation counter for the beta detector has been described by Steyn and Haasbroeck [1958], while a similar unit using a Geiger-Müller counter and liquid scintillation counter for the beta and gamma detectors respectively has been reported by Smith [1954].

A sketch of a $4\pi\beta$–γ coincidence unit as described by Campion (1959) is shown in figure 3.2–1. It consists of a $4\pi\beta$ gas-flow proportional counter having a turntable mechanism to facilitate the loading of sources. Above and below this counter are mounted two 3×3-in. sodium iodide (thallium-activated) crystals and associated electron-multiplier phototubes. The whole detecting system is mounted in a suitable lead shielding, not shown. The use of two crystals, as shown in figure 3.2–1 is, of course, not necessary for β–γ coincidence work. The outputs of the gamma-ray detectors are amplified, pulse-height analyzed and finally added before entering the coincidence mixer.

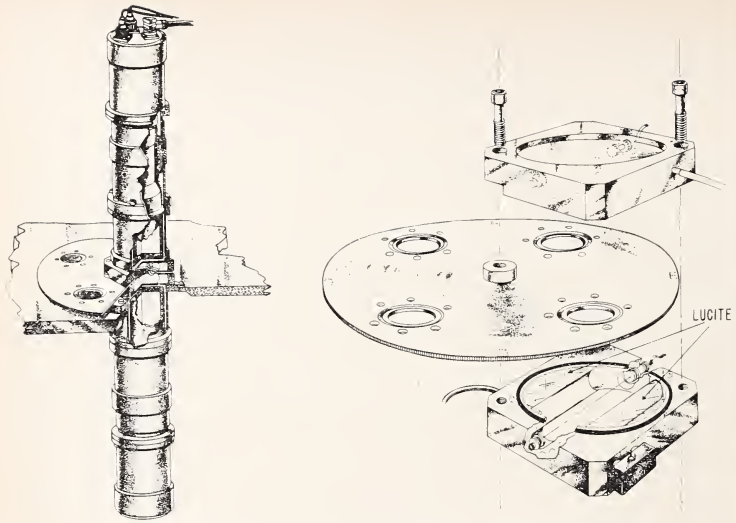


FIGURE 3.2–1. *A $4\pi\beta$–γ coincidence counting unit.*
Left, the complete assembly, excluding shielding. Right, an exploded view of the $4\pi\beta$ proportional gas-flow counter.

In any coincidence arrangement it is essential that no coincidences be lost due to the use of too short a resolving time. A convenient way to check this is to introduce a variable delay in each channel and then to observe the coincidence counting rate as a function of the relative delay between channels. A family of such curves should be obtained for different resolving times. Provided the latter are sufficiently long the curves will exhibit a plateau, the absolute height of which is almost independent of the resolving time. An accurate value of the resolving time, τ_R, can be obtained by introducing completely random pulses into each channel, when the observed coincidence counting rate will be given by eq (3) above.

In $4\pi\beta$–γ coincidence counting N_β is invariably much higher, some 10 to 100 times, than N_γ. In such circumstances it is also important to be certain that the β and γ pulses, arising from the same disintegration, arrive at the coincidence analyzer with no relative delay. Otherwise "instrumental" coincidences [Gandy, 1961] will affect the result.

Only a very brief discussion of the corrections applicable to $4\pi\beta$–γ coincidence counting can be given here, and the reader is referred to Campion [1959] for a more detailed treatment of such corrections. They may, however, be

roughly classified into two groups, (a) those whose relative importance depends on the counting rate and (b) those which do not.

In group (a) there are the random coincidence-rate correction, the dead-time-loss correction, and the background correction.

For high-efficiency detectors the correction for the random, or accidental, coincidence rate is given [Campion, 1959] by

$$N_a \sim \tau_R N_\beta N_\gamma (2-\epsilon_\beta-\epsilon_\gamma). \tag{5}$$

For small values of ϵ_β and ϵ_γ eq (5) clearly reduces to eq (3).

The general expression for the dead-time correction is complex, but it has been discussed in some detail by Campion [1959].

If, however, the dead-times in the individual channels are the same and are equal to τ_D the disintegration rate N_0 can be expressed, in terms of the *observed* counting rates N_β, N_γ and N_c, and neglecting second-order terms, by

$$N_0 = \frac{(N_\beta - N_\beta^{BG})(N_\gamma - N_\gamma^{BG})}{N_c - N_c^{BG}} \left\{ 1 + N_c\tau_D + \frac{2N_\beta N_\gamma - N_c(N_\beta + N_\gamma)}{N_c} \tau_R \right\} \tag{6}$$

where N_β^{BG}, N_γ^{BG}, and N_c^{BG} are the respective background counting rates. N_β and N_γ are the observed counting rates uncorrected for dead-time losses, which have already been taken into account in the derivation of eq (6).

In the second class of corrections, group (b), we have effects due to the angular correlation between the beta and gamma ray, internal conversion of the gamma ray, the sensitivity of the beta detector to gamma-radiation, and the response of the gamma detector to *bremsstrahlung* arising from the slowing down of the beta particles. Since each of these corrections is zero for 100-percent efficiency in the beta counter the advantages of the $4\pi\beta$–γ coincidence method are again apparent.

Finally the case of complex decay schemes has been treated by Wiedenbeck [1947] and Putman [1953]. For such decay schemes it has been shown [Putman, 1953] that the simple expression (2) requires a modifying coefficient which is a function of the efficiencies of the detectors for the various branches. This coefficient is unity provided that the efficiencies of either detector are the same for all branches. For the reasonably high efficiencies obtainable in a $4\pi\beta$ counter,

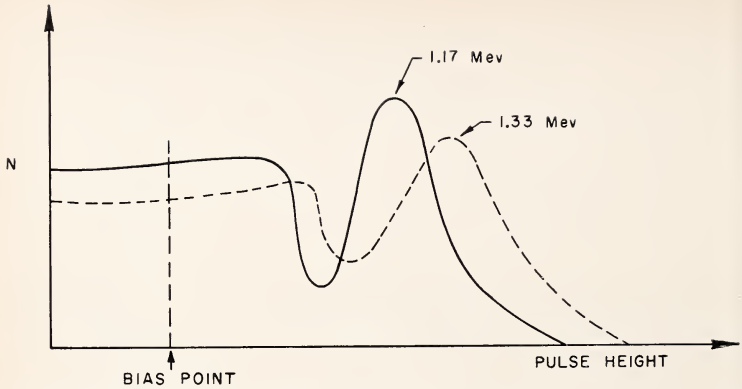


FIGURE 3.2–2. *Integral pulse-height curve for gamma rays of 1.17 and 1.33 Mev.*

this particular coefficient can be neglected for many of the decay schemes encountered.

3.2.2. *Gamma-gamma coincidence counting.* As a second example of the general technique, we shall consider the case of γ–γ coincidence counting. Although this technique is even more limited in application than that of β–γ coincidence counting, it has the advantage that sources in the form of wires or pellets can be readily standardized without the preparation of thin samples such as are required for particle counting.

In the γ–γ coincidence method there are the following important considerations, (a) the relative efficiency of each of the counters for the two gamma rays, (b) possible spurious coincidences due to the Compton scattering of a gamma ray from one counter into the other, (c) possible angular correlation of the gamma rays, and (d) the attenuation of this correlation due to finite geometrical size of the source and counters. The method is perhaps best illustrated by reference to its use in the standardization of cobalt-60 [Hayward, Hoppes, and Mann, 1955].

When two gamma rays of nearly equal energies, such as occur in the decay of cobalt-60, are used, it is impossible to make one counter sensitive only to the first radiation and the other counter sensitive only to the second. In this case it is convenient, by appropriate setting of the bias in each channel, to adjust the efficiencies to be nearly the same for each radiation, as determined by integration under the pulse-height-distribution curve, as shown in figure 3.2–2. The

bias point is chosen so that the areas under the pulse-height-distribution curves are approximately equal. If ϕ_1 is the ratio of the areas for counter 1, and ϕ_2 is the ratio for counter 2, it is easily shown that the coefficient modifying the apparent disintegration rate is

$$F(\phi)=\frac{\phi_1+\phi_2}{(\phi_1+1)\ (\phi_2+1)}. \tag{7}$$

When the ϕ's are equal to unity the coefficient is 0.5. If, for example, the ϕ's are adjusted to no better than 1.2, then the coefficient is 1/2.02; i.e., if a 20-percent error in setting the bias is made, a 1-percent error in the coefficient occurs. With reasonable care, therefore, good accuracy can be achieved.

The setting of the biases by the above criterion usually results in biases so high that spurious coincidences due to scattered gamma rays will be eliminated, except perhaps in situations where the angular separation of the two detectors with respect to the source is small. A 1-Mev gamma ray when scattered through an angle of 90° to 180° is degraded in energy to about 200 kev.

The disintegration rate in terms of observable quantities, neglecting second-order terms and for τ_D small, is given by

$$N_0=\frac{(N_1-N_1^{BG})(N_2-N_2^{BG})}{N_c-N_c^{BG}}\ F(\phi)\ f(\theta)\left(1+2\tau_R\ \frac{N_1\ N_2}{N_c}\right), \tag{8}$$

where N_1 and N_2 are the counting rates in each of two similar detectors, N_c is the coincidence counting rate, $F(\phi)$ is the efficiency coefficient defined above and $f(\theta)$ is a function depending on the geometry [see Feingold and Frankel, 1955] and on any angular correlation between the coincident gamma rays. N_1^{BG}, N_2^{BG}, and N_c^{BG} are the respective background counting rates.

As in the beta-gamma coincidence method described above, the resolving time of the coincidence mixer circuit must be sufficiently long to avoid any loss of true coincidences. The optimum resolving time may be found in a similar way to that in section 3.2.1. Since, however, the random rate is considerably greater in this application, the coincidence counting rate as a function of resolving time exhibits a marked slope above some critical value of the latter. Below this value the curve departs from linearity due to loss of genuine coincidences. The true coincidence counting rate can be found by extrapolation of the linear portion of the curve back to zero resolving time, or by the use of eq (5) above.

3.3. Standardization by Internal Gas Counting

The standardization of low energy beta emitters presents a special problem because of the relatively large self-absorption associated with $4\pi\beta$ counter sources prepared in the usual manner. This problem may be eliminated by adding the sample, in gaseous form, to the counting gas of a proportional or Geiger-Müller counter of known physical dimensions [Miller, 1947; Brown and Miller, 1947; Anderson, Libby, Weinhouse, Reid, Kirschenbaum, and Grosse, 1947; Engelkemeir, Hamill, Inghram, and Libby, 1949; Curran, Angus, and Cockroft, 1949; Jones, 1949; Mann and Parkinson, 1949; Hawkings, Hunter, and Mann, 1949; Bernstein and Ballentine, 1950; Engelkemeir and Libby, 1950; Jones, 1951; Rieck, Myers, and Palmer, 1956; Mann, 1958; Merritt and Hawkings, 1960]. The method is also applicable to Auger electrons of electron-capturing nuclides.

The weakening of the field at the counter ends, and beta particles entering the counting volume from the "dead" ends, make corrections necessary, or these can be eliminated by using a set of two or three counters of different length but of the same cross section. The ends with the supports for the anode wire should be of identical construction. By taking differences in counts between any pair of counters, the end effects cancel.

Wall effects can be determined by extrapolation of the observed counting rate as a function of inverse pressure to zero inverse pressure. Some experimenters have also varied the diameter of their counters, leaving the pressure constant.

3.4. The Calorimetric Method

Microcalorimeter methods have recently been used at the National Bureau of Standards both for the intercomparison of national radium standards and for the standardization of artificially produced radionuclides and polonium-210.

The twin-cup compensated microcalorimeters which were built for this purpose [Mann, 1954a and 1954b] use the Peltier-cooling effect to balance the energy emission of the radioactive source.

The National Bureau of Standards radiation balance, as this twin calorimeter has been called, has been used to prepare standards of tritium, of sulfur-35 [Seliger, Mann, and Cavallo, 1958] and to calibrate a polonium-210 source in connection with the measurement of the branching ratio in the decay of polonium-210 [Hayward, Hoppes, and Mann, 1955]. A knowledge of this ratio, namely 1.22×10^{-5} gamma quantum per alpha particle, enables a strong polonium-210

source to be assayed simply by measurement of the number of 0.804-Mev gamma rays from the daughter nucleus, lead-206. It has also recently been used to prepare a new series of radium solution standards [Mann, Stockmann, Youden, Schwebel, Mullen, and Garfinkel, 1959]. A precision of about 0.1 percent is achieved in calibrating a radium source in terms of the national radium standards, but the standardization of an alpha- or beta-emitting nuclide depends on a knowledge of the energy of the alpha particles or the average energy of beta decay.

A twin calorimeter has also been developed at Atomic Energy of Canada Limited [Bayly, 1950] and used for the standardization of a phosphorus-32 source. This calorimeter was based on the principle of balancing the temperature rise in the cup containing the radioactive source by adjusting the current in an electrical heating coil in the twin cup so that there is no temperature difference, measured by a thermistor in each cup, between the two cups. In common with the National Bureau of Standards radiation balance, it was found necessary to place the calorimeter in a temperature-attenuating enclosure, but, in contrast to the radiation balance, it was found necessary also to maintain the room containing the calorimeter at a temperature which was constant to within ± 0.05 °C.

The measurement of the disintegration rate of the phosphorus-32 source was made with an estimated "absolute error" of ± 2 percent.

3.5. Liquid Scintillation Counting

Liquid scintillation counting, like internal gas counting, eliminates the problem of source self-absorption. In this method, the material is incorporated into a liquid scintillating solution and the light pulses produced are counted by means of either a single electron-multiplier phototube, or two in coincidence. Thus far the technique is not considered suitable for the absolute counting of beta particles below about 5 or 10 kev because an insufficient number of photons is produced, having due regard to the efficiency of light collection and also to the efficiency of ejection of photoelectrons at the photocathode.

Basson and Steyn [1954] have standardized alpha-particle solutions of polonium-210 by incorporating the solution directly into the liquid scintillator, and Steyn [1956] and Seliger [1958a and 1958b] have extended this technique to the standardization of beta-emitting nuclides.

The method of $4\pi\beta$-liquid-scintillation counting using solid sources has been used in the standardization of alpha and

beta emitters [Belcher, 1953; Basson and Steyn, 1954; Steyn, 1956; Seliger, 1958a and 1958b]. For beta emitters, Belcher [1953] supported the source in the liquid scintillator between a sandwich of two thin foils. The absorption correction for these foils and for source self-absorption can, however, be quite high.

3.6. Standardization of Gamma Emitters by Dosimetry

If the decay scheme and disintegration rate of a radionuclide are known, the gamma-ray dose rate at a given distance can be calculated. Conversely, the disintegration rate of the source can be deduced from a measurement of the dose rate at a known distance.

The rate, ϵ, at which energy from the gamma radiation is transferred to kinetic energy of secondary electrons per unit mass of material at distance d, assuming that there is no absorption in the intervening distance, is given by

$$\epsilon = \frac{N \Sigma_k n_k \, {}_m\mu_{en k} E_k}{4\pi d^2} \tag{1}$$

where N is the disintegration rate of the source, n_k is the fraction of disintegrations in which a photon of energy E_k is emitted, and ${}_m\mu_{en k}$ is the mass energy absorption coefficient of the medium for radiation of photon energy E_k. In eq (2)

$${}_m\mu_{en} = {}_m\sigma_a + {}_m\tau_a + {}_m\pi_a \tag{2}$$

where ${}_m\sigma_a$ is the Compton mass absorption coefficient, and ${}_m\tau_a$ and ${}_m\pi_a$ are the mass photoelectric and pair production coefficients reduced by the fraction of the photon energy re-emitted respectively as characteristic X rays and annihilation radiation.

In circumstances where the gamma-ray intensity does not vary appreciably over the region from which secondary electrons reach the point at which the dose rate is measured, the energy ϵ can be equated to the energy locally absorbed.* Hence, under these conditions, which are usually not difficult to satisfy, eq (1) gives the absorbed dose rate in the medium. Thus, any dose meter which is valid over the range of gamma-ray energies emitted can, in principle, be used to determine the disintegration rate of the source. By such means a useful and rapid standardization can often be carried out in laboratories lacking the equipment for the more direct methods.

*Strictly, the energy absorbed is less than ϵ by the quantity of energy re-emitted by the secondary electrons as *bremsstrahlung*. This quantity is usually very small.

Most systems for measuring gamma-ray dose respond to the absorbed dose in the medium—the chamber walls in the case of a cavity chamber—rather than to the exposure dose. However, the exposure dose can usually be derived readily from the measurement, and many instruments are, of course, calibrated to read directly in roentgens. When the material irradiated is air, eq (1) becomes essentially an expression for the *exposure dose rate.* The exposure dose measures the exposure in terms of the production of secondary electrons in a standard mass of air, and measures these latter in terms of the ionization they produce. Since the average energy expended in the production of an ion pair in air (W_{air}) is virtually independent of the energy of the secondary electron, an exposure dose of 1 roentgen corresponds to the transference of the same quantity of photon energy in unit mass of air, irrespective of the quantum energy of the gamma rays. The relation between the exposure dose rate R and the quantity ϵ, specified by eq (1), is

$$R=\frac{\epsilon}{W_{air}}\times 6.21\times 10^{-13}\ \mathrm{r\ sec^{-1}}. \tag{3}$$

The International Commission on Radiological Units and Measurements suggests the use of 34 ev for W_{air} (ICRU–NBS Handbook 78). This value is probably accurate to 3 percent and may be used with gamma-ray energies greater than 20 kev. From eq (1) and (3) one can derive the *specific gamma-ray emission,* Γ (ICRU–NBS Handbook 78):

$$\Gamma=1.50\times 10^{5}\Sigma_k n_k \mu_{air_k} E_k\ \mathrm{r\ h^{-1}\ mc^{-1}\ at\ 1\ cm}, \tag{4}$$

where μ_{air} is the *linear* absorption coefficient in air (fig. 3.6–1) and E is in Mev.

The specific gamma-ray emission is shown as a function of gamma-ray energy in figure 3.6–2, and is tabulated for certain radionuclides in appendix A. It should be noted that Γ does not include the effect of characteristic X rays and *bremsstrahlung.* A correction must be applied to measurements on radionuclides in which there is an appreciable contribution from these radiations. Over the range 0.07 to 1.8 Mev, the absorption coefficient is approximately constant and

$$\Gamma\simeq 5.25\ E\ \mathrm{r\ h^{-1}\ mc^{-1}\ at\ 1\ cm} \tag{5}$$

where E is the average total gamma-ray energy in Mev per disintegration.

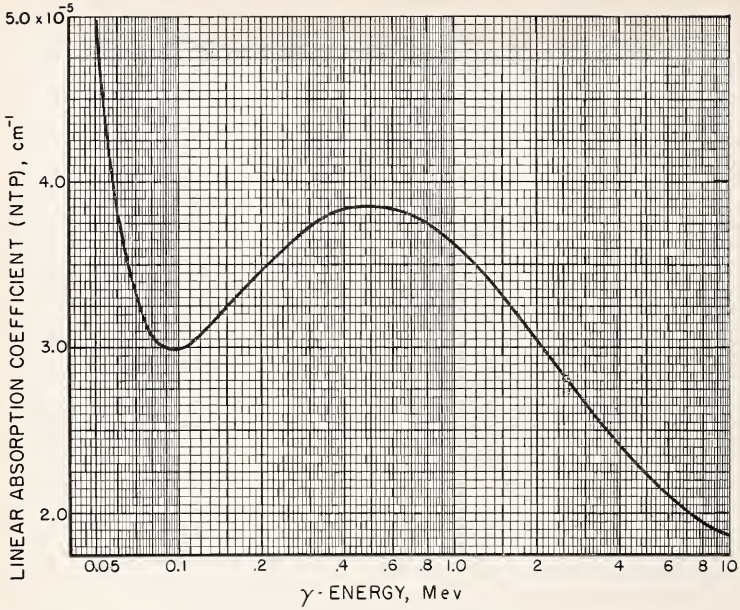


FIGURE 3.6–1. *Linear energy absorption coefficient for photons in air at NTP.*

[From ICRU–NBS Handbook No. 62, 1956.]

If the exposure dose rate is measured, the activity of the source is given by:

$$S = \frac{Rd^2}{\Gamma} \text{ mc}, \tag{6}$$

where R is the exposure dose rate in r h^{-1} (The disintegration rate, N, is $3.7 \times 10^7 \times S$ d.p.s.)

If the absorbed dose rate is measured it may still be convenient to make use of the tabulated values of Γ. The energy removed from the photon radiation per gram of material is given by

$$\epsilon = 88 \frac{\Gamma}{d^2} \left(\frac{{}_m\mu_{en}}{{}_m\mu_{en\ air}} \right) \text{ erg/mc h}, \tag{7}$$

and in conditions of electronic equilibrium this will be equal to the absorbed dose rate. (Values of ${}_m\mu_{en}$ are given in table 8.1 of ICRU–NBS Handbook 78). In light materials such as carbon and plastics, absorption is almost wholly by Compton collisions over the energy range 0.3 to 1.5 Mev. The ratio of the coefficients, ${}_m\mu_{en}/{}_m\mu_{en\ air}$ is then virtually a constant, the ratio of the electron densities in the two media.

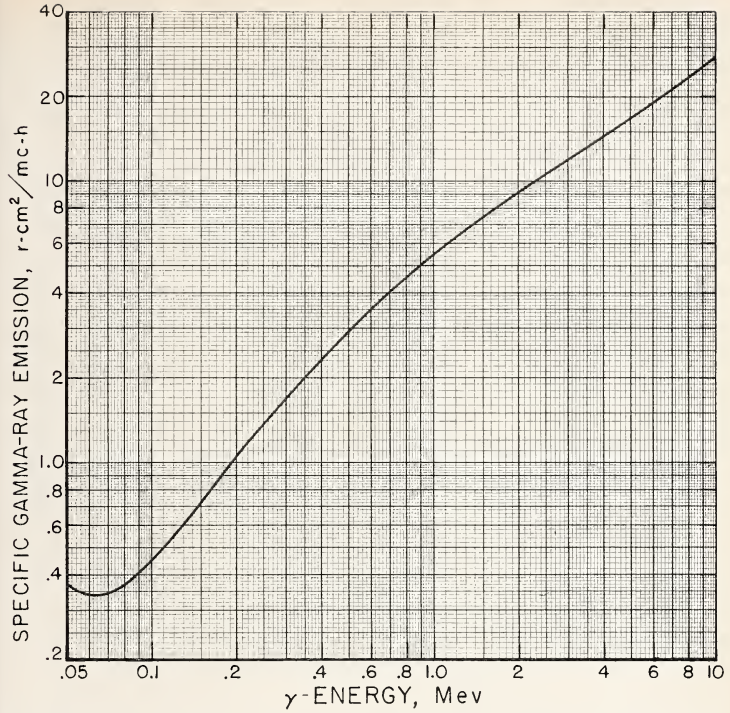


FIGURE 3.6–2. *Specific gamma-ray emission* Γ *for a point source assuming one photon of energy* E_γ *per disintegration.*

At higher or lower energies, pair production or photoelectric absorption become appreciable and must be taken into account. In these circumstances the calibration factor of a dosimeter in terms of exposure dose is likely to be energy dependent, and one should be cautious in calibrating a source against another of known gamma-ray emission but of different photon energy. It is assumed that, where necessary, proper corrections are made for the attenuation of the gamma radiation by absorption in the source, the intervening air and the walls of the dosimeter, and for the effect of scattered radiation.

The disintegration rate of some radionuclides is very difficult to measure directly because of uncertainties in the decay scheme. In such cases, as for example cesium-137, the dosimetry method is particularly useful for providing standards based on gamma-ray emission.

3.6.1. *Measurement by ionization chamber.* The use of an ionization chamber for the determination of disintegration rate has been described in detail by Gray [1949]. The rate at which energy is absorbed within the air of a cavity chamber can be calculated from the ionization produced, assuming a value for W_{air}. If the cavity is small enough to produce no appreciable disturbance of the secondary electron flux generated by the gamma rays irradiating the surrounding medium, the energy absorption per gram in the medium is related to that in the air by the stopping power of the medium relative to air. If the chamber walls are thick enough to attain "electronic equilibrium" this rate of energy absorption is given in terms of the disintegration rate of the source by eq (1). The disintegration rate is thus expressed in terms of the ionization current. An absolute measurement involves accurate determination of the source-to-chamber distance, chamber volume, air density and absolute ionization current; allowances must be made for absorption of the gamma rays in the source, chamber wall and intervening air, and for the relative stopping power. The measurement of effective distance presents no great difficulties; the inverse square law holds good until the distance is only a few times the chamber dimensions [Sinclair, Trott, and Belcher, 1954]. Dependence on the distance can be eliminated entirely by using a spherical "extrapolation" chamber surrounding the source [Gross, Wingate, and Failla, 1957]. Absorption within the source can be allowed for by the methods of Evans and Evans [1948]. Absorption in the chamber walls can be estimated from observation of the effect of increasing the wall thickness. There is an uncertainty however, leading to an error which is usually less than 1 percent, in deciding the wall thickness to which the observation should be extrapolated—for the secondary electrons arise from varying depths within the walls. [See, for instance, Attix and Ritz, 1957.] The correction for relative stopping power can be made quite small by choosing a wall material whose atomic number is close to air. Carbon is often used for this purpose. Fairly good corrections have been derived from observations with chambers having wall materials of different atomic numbers, by interpolating to find the value for a chamber whose walls have the same mean atomic number as air. This procedure assumes that stopping power is a smoothly varying function of Z only, which is not strictly true. A thorough treatment of the problem is quite complicated, and involves consideration of the effects of the density of the medium and the size of the cavity. [NRC–NBS Handbook 79]

The calibration is altogether simpler if it is made relative to a standard of known gamma-ray emission, similarly situated relative to the chamber. The comparison gives a value of the exposure dose at standard distance from the source, and the disintegration rate is found in terms of Γ. Only a ratio of ionization currents is required. A correction for self-absorption must be made, but the only corrections for chamber-wall absorption and relative stopping power arise from the differences in these quantities between source and standard, and, except at low energies, are usually less than 1 percent [table 3.6–1]. Radium standards are most commonly used for this purpose, since accurately standardized sources are widely available and of long half-life. The gamma-ray spectrum of radium is not accurately enough known to admit of a satisfactory calculation of Γ; but recent experimental values are 8.26 [Attix and Ritz, 1957] and 8.24 [Henry, 1957] roentgens per hour at 1 cm from 1 mg of radium in equilibrium with its decay products when enclosed in 0.5 mm of platinum.

TABLE 3.6–1. *Typical correction factors for ionization-chamber γ-ray measurements*

Radionuclide	Absorption in typical ampoule	Chamber wall absorption relative to radium	Overall correction factor
Tm^{170}	1.07	1.10	1.18
I^{131}	1.025	1.025	1.05
Br^{82}	1.02	1.00	1.02
Co^{60}	1.02	1.00	1.02
Na^{24}	1.015	1.00	1.015

In carrying out ionization-chamber measurements care should be taken that the wall thickness is sufficient not only to give electronic equilibrium but also to exclude beta rays from the source. It should also be borne in mind that some commercial ionization chambers are not truly "air equivalent" over a wide energy range, and correction for this may have to be applied [Szilvasi and Whyte, 1959]. The operation of ionization chambers is also discussed in sections 2.1 and 7.2.

3.6.2. *Measurement of dose by Geiger-Müller counter.* For ionization-chamber measurements, sources of the order of several millicuries are needed. Such a strength is often well above that of preparations used for clinical applications. The Geiger-Müller counter is a more sensitive device and is, under certain conditions, suitable for measuring exposure dose [Sinclair, 1950; Hine and Brownell, 1956, ch. 11, "Standardization of X-ray Beams and Radioactive Isotopes", W. K. Sinclair].

The photon efficiencies for Geiger-Müller counters are given in figure 3.6–3. It will be noted that for a wide energy range the copper-wall counter exhibits an efficiency which is nearly proportional to the photon energy. Since in the approximate eq (5) the specific gamma-ray emission is proportional to the photon energy, one would expect the counting rate of a copper counter to be proportional to the exposure dose rate. This is shown in figure 3.6–4, where the number of counts per cm^2 of effective cathode area is given for an exposure dose of 1 roentgen for various wall materials. A flat response to an accuracy of ± 15 percent can be achieved for a brass (copper) counter within an energy range of from 0.3 to 3.0 Mev. Although it is possible, by using figure 3.6–4, to calculate the response of a Geiger-Müller counter of known cathode area, it is more advisable to calibrate the counter with a source of known gamma-ray emission. This method is very simple to use for a rough determination of source strength and is applicable to gamma emitters in the microcurie range.

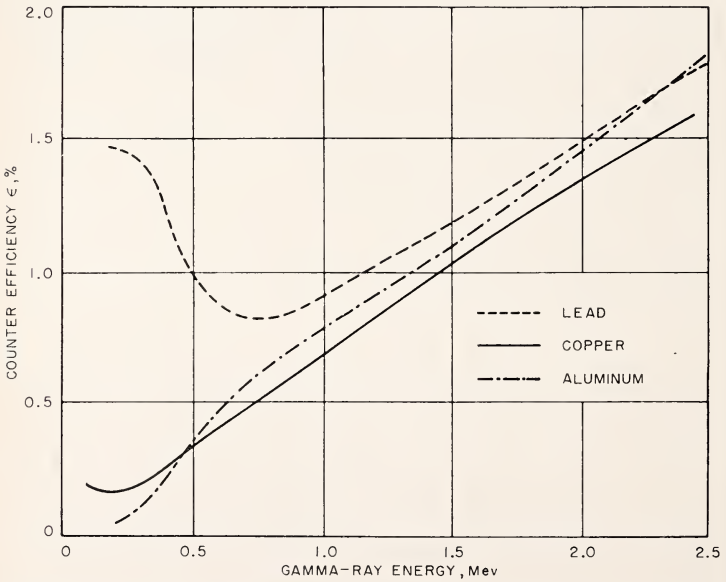


FIGURE 3.6–3. *Intrinsic counter efficiency as a function of gamma-ray energy in Geiger-Müller counters with different cathode materials.*

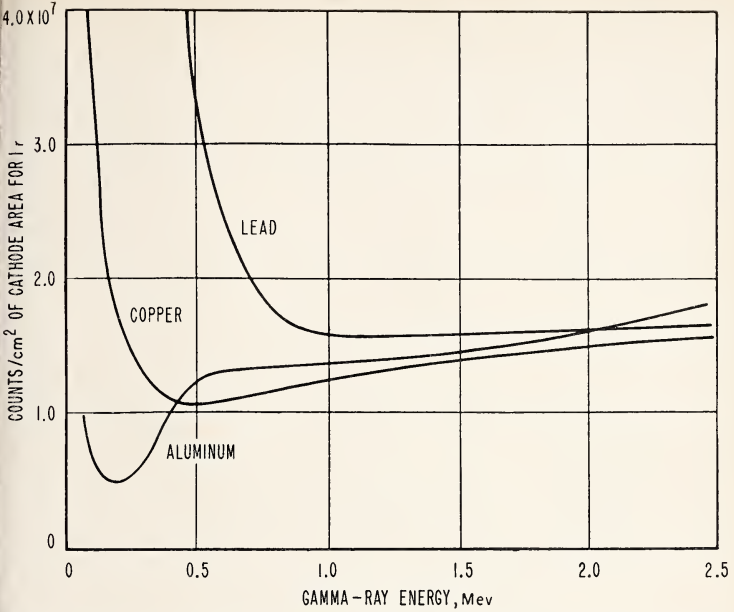


FIGURE 3.6–4. *Response of Geiger-Müller counters of different cathode materials in terms of gamma dose in roentgens.*

[Hine and Brownell, 1956, ch. 5, Geiger-Müeller counters and proportional counters, W. K. Sinclair; courtesy of Academic Press.]

3.7. Standardization of Beta Emitters by Dosimetry

In a medium throughout which a beta-emitting substance is uniformly distributed the absorbed dose rate is uniform and equal to the rate at which beta-ray energy is emitted per gram of the medium. The disintegration rate is thus determined in terms of the measured dose rate and the mean energy of the beta rays. This mean energy is often available from spectrometer studies or can be reliably calculated from the maximum energy and a knowledge of the type of spectrum involved [Loevinger, 1957 and ICRU–NBS Handbook 78; see also appendix A]. The condition that the dosimeter should not interfere with the dose rate in the medium is much more stringent than with gamma rays, where secondary electrons emitted from the dosimeter largely compensate for those absorbed from the surrounding medium. A chemical dosimeter system incorporated in the medium should, in

principle, be suitable. Gray [1949] has used a cavity ionization chamber lined with active material, and allowed for absorption in the air of the cavity by extrapolating, to zero pressure, the ratio of ionization current to air pressure. Others [Failla, Rossi, Clark, and Bailey, 1947; Sommermeyer, 1952] have used chambers of the "extrapolation" type [Failla, 1937, Bortner, 1951]. If the radionuclide emits gamma rays it may be difficult to assess their contribution to the observed dose rate accurately.

This method of standardization is seldom used: it is practicable only with fairly energetic beta rays, for which 4π beta-ray counting is more suitable.

3.8. Loss-of-Charge Method

Measurements of the charge carried away from a source of radium have been made by several investigators [Wien, 1903; Rutherford, 1905; Makower, 1909; Moseley, 1912]. Recently, however, this method has been applied to the standardization of beta-emitters [Clarke, 1950; Gross and Failla, 1950; Keene, 1950]. Using a spherical geometry, Clarke [1950] achieved agreement with National Bureau of Standards measurements of standard samples of phosphorus-32 to within 5 percent, but the method has not since been in general use. Gross and Failla [1950] used a parallel-plate geometry where the source was a very thin deposit of the emitter in question on one plate of a parallel-plate collecting system, the second plate being sufficiently close to balance the secondary electron emission and backscattering effects. Low-energy secondary electrons were bent back by means of a weak magnetic field, and the measurement was made in a vacuum to eliminate air ionization. Agreement with the National Bureau of Standards measurements of standard samples of phosphorus-32 to within ± 2 percent has been obtained by this method by Gross and Failla over a number of years [Seliger and Schwebel, 1954]. In another development of the charge-measuring method [Keene, 1950], the source was deposited on a thin aluminum foil that was completely surrounded by an open-mesh wire-grid enclosure. This experiment, like the first, was carried out in a vacuum, and the current from the foil to the grid was measured for different positive and negative voltages between them. Using a phosphorus-32 source, agreement to about 10 percent with an activity measurement by the Atomic Energy Research Establishment was quoted.

3.9. Calculation of Activity of Artificially Produced Radionuclides From Irradiation Data

The disintegration rate of radionuclides produced by bombardment with neutrons or charged particles may be calculated if the cross section of the target nuclide (stable) and the flux of bombarding particles are known [Hughes, 1953; Halliday, 1955]. Neutron reactions only will be considered here, since their treatment is typical of particle bombardments.

"Slow" neutrons in a reactor are most often used for "activation." Neutron flux is usually determined by use of a "monitor" containing a known amount of a nuclide whose thermal activation cross section is well established. Cobalt (36.3 barns), gold (98.8 barns), and manganese (13.3 barns) are convenient standards. A tabulation [Hughes and Schwartz, 1958] of cross sections is available.

For calculation of the neutron flux by use of the monitor, one may use the equation

$$f=\frac{A_m}{N_m\sigma_m e^{-\lambda_m t_d}(1-e^{-\lambda_m t_b})}, \tag{1}$$

where f=flux, in cm^{-2} sec^{-1},
A_m=disintegration rate of monitor, in sec^{-1},
N_m=number of atoms of stable monitor nuclide,
σ_m=thermal activation cross section of monitor nuclide, in cm^2,
λ_m=decay constant of activity, in sec^{-1},
t_d=time between bombardment and measurement, in seconds, and
t_b=bombardment time, in seconds.

Now, the disintegration rate of the desired radionuclide produced in the bombardment may be calculated from the relation

$$A=N\sigma f e^{-\lambda t_d}(1-e^{-\lambda t_b}), \tag{2}$$

where terms have the same significance as before. The introduction of the sample must not affect the flux distribution appreciably.

In general, the use of bombarded samples as standards is not as accurate as most of the methods previously discussed, chiefly because of uncertainty in knowledge of the energy distribution of neutrons in reactors. The usually well known thermal neutron cross section therefore has to be modified to include activation by epithermal or fast neutrons. Further, it is necessary to measure the disintegration rate of the monitor; such standards, might therefore, be considered to be derived standards.

4. Methods of Relative Standardization as Carried Out in Standardization Laboratories

4.1. General

In the national standardizing laboratories a standardization of any radionuclide (particularly a short-lived radionuclide) is usually preserved by using a standardized source to calibrate a reference instrument such as an ionization chamber. This instrument can then be used to calibrate further samples of the same radionuclide to give derived or "secondary" standards at any later date, or to check the consistency of subsequent absolute standardizations. The stability of the instrument is usually checked by measuring a reference source of some long-lived material, such as radium, whenever a calibration is made. One may either take the activity of the sample to be proportional to the response of the instrument (having checked its stability), or to the ratio of the response to that produced by the reference source (in which case variations in the sensitivity of the instrument are immaterial so long as they affect the responses to both sources equally).

The methods of relative standardization described in the following sections may sometimes be similar to those employed by the user of radioactive materials. Such methods are discussed in sections 7.1 through 8.2.

The simplest way of effecting a comparison between an absolute (or "primary") and relative (or derived or "secondary") standard of radioactivity is to measure, by means of a substitution method under reproducible conditions, the relative activities using any instrument that records either individual beta or gamma rays or else measures their ionizing effects. Such a method, whatever the nature of the recording device, can be relied upon to give relative values having a standard deviation of from 0.03 to 1.0 percent, which is usually less than the uncertainty with which the activity of the absolute standard is known. It is also to be understood that within the meaning of "reproducible conditions" is to be included the geometry of the equipment and the disposition and quantity of any material absorbing or scattering the radiations. In these respects the characteristics of the source itself are no less important than those of the measuring instrument.

The method of comparing unknown sources of beta-emitting nuclides with a calibrated radium D+E source and an end-window counter [Mann and Seliger, 1958a] is no longer very acceptable, because the geometrical conditions are, on

the whole, somewhat irreproducible and involve considerations of absorption and backscattering. The method has, however, been shown to give consistent results with the use of "weightless" sources mounted on thin films [Novey, 1950]. In general, radium D+E sources are now recommended only for use as reference sources for the maintenance of the calibration of measuring equipment by the method of substitution in which the initial calibration has been made using a standard sample of the radionuclide in question. Even in this limited context, however, uncertainty of the half life of radium D makes it desirable to substitute radium itself for long-term use.

The recording device used in such a substitution method can be a gold-leaf or quartz-fiber electroscope; a beta-ionization chamber or gamma-ionization chamber used in conjunction with a Lindemann-Ryerson, or vibrating-reed electrometer, or any other low-current-measuring device; any kind of beta-, gamma-, or X-ray counter; or a formamide solution in a $2\pi\beta$-proportional counter.

Some of the methods of relative standardization described in this section are also discussed in sections 7.1 through 8.2.

4.2. Ionization Chambers

At the National Bureau of Standards, the absolute standardizations of the short-lived radionuclides were maintained for several years by means of a $2\pi\beta$-ionization chamber in conjunction with radium D+E reference sources, and a $4\pi\gamma$-ionization chamber in conjunction with reference standards of radium consisting of radium bromide solution in flame-sealed glass ampoules [Seliger and Schwebel, 1954]. More recently, both types of reference sources have been replaced by radium sources, with the radium salt sealed in platinum-iridium cells, which in turn are encapsulated in stainless steel disks for use in the $2\pi\beta$ chamber, and in polystyrene cylinders to simulate the geometry of the ampoules containing liquid. Absolute or national standards of the short-lived radionuclides sodium-24, phosphorus-32, potassium-42, iodine-131, and gold-198 are calibrated by $4\pi\beta$ or coincidence counting. These absolute standards are then used to effect a calibration of the appropriate ionization chamber in conjunction with a radium reference source. Relative (or derived or working) standards of these artificially produced radionuclides can then be calibrated against the appropriate reference sources in these chambers (drawings of the two NBS chambers are given in Mann and Seliger, 1958a).

In an ionization chamber the density of the gas must be kept constant, or a correction must be made for any change (due to change in temperature or pressure). In a gamma-ray chamber whose walls have an atomic number near to that of the gas, the response will be closely proportional to the density of the gas. In a beta-ray chamber, or a gamma-ray chamber in which there is a substantial effect from photoelectrons originating in the walls, the fractional change in current will be rather less than the fractional change in density. In the most accurate work it may be necessary to take this fact into account, and it may be desirable to design the chamber so that the gas pressure can be varied to permit investigation of the dependence of response on gas density.

Ionization chambers, particularly those used in conjunction with a vibrating-reed electrometer or other very sensitive device for measuring extremely small electric currents, are very useful for assaying gas samples, and are often used for comparing the activities of hydrogen-3 and carbon-14 in the gas phase [Tolbert, 1956 and 1958]. The gas sample is admitted quantitatively into the evacuated chamber and the resulting ionization current measured. This method is used chiefly as a comparative method; i.e., the ionization current of the unknown sample of gas is compared with that of a sample of gas prepared in the same way and containing a known amount of the radioactive nuclide [Marlow and Medlock, 1960]. Absolute calibrations have also been carried out by this method [Wilzbach, Van Dyken, and Kaplan, 1954; Rieck, Myers, and Palmer, 1956; Tolbert, 1956 and 1958].

4.3. Solution Counting

Several radionuclides have been successfully counted in solution, using an inert, low-vapor-pressure solvent such as formamide, dimethyl formamide or ethylene glycol [Schwebel, Isbell, and Karabinos, 1951; Schwebel, Isbell, and Moyer, 1954]. This sample is dissolved in the inert solvent and an aliquot is pipetted into a cupped planchette. The activity is then measured in a $2\pi\beta$ windowless gas-flow counter, and compared with the activity of a solution prepared in the same manner, but containing a known amount of the radionuclide (for sample preparation, see sec. 5.4.1).

This "formamide" counting procedure has so far been found useful for the relative standardization of carbon-14 as glucose and benzoic acid, phosphorus-32 as sodium phosphate, cobalt-60 as cobalt chloride, strontium-yttrium-90

in strontium chloride, iodine-131 as potassium iodide, thallium-204 as thallic nitrate, sodium-22 and sodium-24 as sodium chloride, and sulfur-35 as sulfuric acid.

For any given counter and cell it is possible also to obtain relative efficiencies for the above radionuclides. These efficiencies may then be used to assay any of these radionuclides in terms of, say, a carbon-14 source.

Proportional or Geiger-Müller counters of the dipping or jacketed type may also be used to assay aqueous solutions.

4.4. Liquid Scintillation Counting

For low energy beta emitters, such as hydrogen-3 or carbon-14, comparisons with absolute standards can be carried out by liquid scintillation counting [Raben and Bloembergen, 1951; Audric and Long, 1952 and 1953; Ziegler, Seliger, and Jaffe, 1956; Steyn, 1956, Seliger and Ziegler, 1957]. Hydrogen-3 standards, in the form of tritiated water, were distributed in 1953 by Atomic Energy of Canada Limited to a number of laboratories for intercomparison. At the National Bureau of Standards the Canadian and United States standards were compared by the method of liquid scintillation counting and found to agree to within 1.3 percent. The Canadian standard had been calibrated by the method of gas counting [Hawkings and Merritt, 1954] and that of the United States, calorimetrically [Mann and Seliger, 1958a]. (For sample preparation, see sec. 5.4.2.)

Recently a method has been developed for scintillation counting of biochemical compounds having limited solubility in organic solvents [Steinberg, 1958 and 1959]. This method is based on the use of a two-phase system consisting of the scintillator in the form of numerous glass or plastic rods or beads, and a liquid phase containing the radioactive material that is to be assayed.

Recent publications [Davidson and Feigelson, 1957; Bell and Hayes, 1958], discuss the theory, techniques, and applications of liquid scintillation counting and review progress in this field through 1957.

4.5. Gel Scintillation Counting

Carbon-14-labeled barium carbonate of low specific activity has also been counted in a thixotropic scintillator gel with 56-percent efficiency [Nathan, Davidson, Waggoner, and Berlin, 1958]. (For preparation, see sec. 5.4.3.)

5. Techniques of Preparing Standard Solutions and Samples for Counting

5.1. Standard Solutions

Most radionuclide standards are in the form of salts dissolved in suitable carrier solutions and contained in flame-sealed glass ampoules. For these the same general considerations apply as are outlined in section 1.4. The concentration of inactive carrier and the pH of the solution are adjusted to minimize loss of activity due to adsorption and loss of homogeneity due to precipitation. In some cases, notably tantalum-182 and gold-198, it has been found that long-term stability is a problem and that special chemical formulations, different from those in which the material is received, are required. The carrier solution for the radioactive nuclide is usually prepared from a compound of its stable isotopes, usually in the same chemical form. The minimum amount of carrier which should be used will have to be obtained from experience. Table 5.1–1. gives the chemical data for various radionuclide solution standards as preferred by the National Bureau of Standards. This table may also serve as a guide for the preparation and dilution of radioactive solutions. (For storage of solutions, see Preiss and Fink, 1957.)

5.2. Dry Samples

The most common method of preparing a source for β-, X-ray or coincidence counting is to deposit a known volume or weight of the radioactive solution upon a source mount and to evaporate to dryness in air. This simple technique is suitable for the higher energy beta-emitters, but even for gold-198 (maximum beta energy 0.96 Mev) difficulties arise from source self-absorption. Current experiments, however, indicate that losses due to absorption in the source material can be reduced to a minimum by employing certain techniques in the preparation of solutions and sources; e.g., in the measurement of the activity of sulfur-35, a weak β emitter ($E_{\max}$=0.167 Mev), very dilute acids are used, and Ludox is added to the sources which are dried in air, then placed in an oven at 70° C for several days.

Methods to reduce self-absorption have also been discussed in section 3.1.4. and techniques for preparing suitable sources for $4\pi\beta$ proportional counting are listed in the last column of table 5.1–1.

TABLE 5.1–1. *Source-preparation techniques and chemical data on standard solutions used at the National Bureau of Standards*

Radionuclide	$E_{\beta max}$.	Ionic form	Carrier solution	Approximate inactive to active ion ratio	Method of preparation of $4\pi\beta$ PC sources
H^3	0.018	H^+	H_2O	9×10^9	
C^{14}	0.16	$[CO_3]^{--}$	10.621 g/liter Na_2CO_3 and 0.120 g/liter NaOH in H_2O.	2×10^6	
Na^{22}	0.54	Na^+	0.10 g/liter NaCl in 1*N* HCl.	6×10^5	Freeze-dried, redissolved in H_2O, freeze-dried.
Na^{22}	0.54	Na^+	2.0 g/liter $NaNO_3$ in 1*N* HNO_3.	9×10^5	Ludox* added, dried in air, then heated under infrared lamp.
Na^{24}	1.39	Na^+	0.10 g/liter NaCl in 1*N* HCl.	2×10^7	Ludox added, dried in air, then heated under infrared lamp.
P^{32}	1.71	$[PO_4]^{---}$	0.098 g/liter H_3PO_4 in H_2O.	3×10^6	Ludox added, dried in air.
S^{35}	0.167	$[SO_4]^{--}$	0.1*N* HCl	10	Ludox added, dried in air, then placed in oven at 70 °C for several days.
K^{42}	3.54	K^+	0.10 g/liter KCl in 1*N* HCl.	10^7	Ludox added, dried in air.
Fe^{55}		Fe^{+++}	0.001 g/liter $FeCl_3$ in 1*N* HCl.	2×10^2	
Co^{60}	0.31	Co^{++}	0.01 g/liter $CoCl_2$ in 0.1*N* HCl.	2×10^5	Dried in desiccator, redissolved in conductivity H_2O and dried in NH_3 atmosphere.
Zn^{65}	0.32	Zn^{++}	0.5 g/liter $ZnCl_2$ in 6*N* HCl.	4×10^3	
Kr^{85}	0.67		Inert krypton	2×10^{16}	
Sr^{90}–Y^{90}	0.54 Sr^{90}	Sr^{++}	0.027 g/liter $SrCl_2.6H_2O$	9×10^3	Dried in air, redissolved with 0.001*M* H_3PO_4, dried, redissolved with H_2O and dried in NH_3 atmosphere.
	2.23 Y^{90}	Y^{+++}	and 0.022 g/liter $YCl_3\cdot6H_2O$ in 1*N* HCl.	3×10^7	
I^{131}	0.81	I^-	0.020 g/liter LiOH, 0.020 g/liter Na_2SO_3 and 0.050 g/liter KI in H_2O.	2×10^6	$AgNO_3$ solution added immediately to deposit of I^{131}.

*Colloidal silica.

TABLE 5.1–1. *Source-preparation techniques and chemical data on standard solutions used at the National Bureau of Standards*—Con.

Radionuclide	$E_{\beta max}$.	Ionic form	Carrier solution	Approximate inactive to active ion ratio	Method of preparation of $4\pi\beta$ PC sources
Cs^{137}–Ba^{137}	1.18 Cs	Cs^{+} Ba^{++}	2.0 g/liter CsCl in 1*N* HCl.	5×10^{3}	Ludox added, dried in air, and then heated under infrared lamp for several days.
Pm^{147}	0.225	Pm^{+++}	1 *N* HCl	------	Ludox added, dried in air, placed in desiccator (NaOH), then heated under infrared lamp for several days. Redissolved with conductivity water, dried in air, replaced in desiccator under infrared lamp for at least one week.
Ta^{182}	0.510	$[TaF_7]^{--}$	Very dilute HF	10^{5}	Dried in air, redissolved with H_2O, redissolved again with H_2O and dried in NH_3 atmosphere.
Au^{198}	0.96	$[Au(CN)_4]^{-}$	0.1g/liter $KAu(CN)_4$ and 0.001g/liter KCN.	9×10^{6}	Ludox added, dried in air.
Tl^{204}	0.77	Tl^{+++}	0.017 g/liter $Tl(NO_3)_3$ in 1*N* HNO_3.	2×10^{4}	Ludox added, dried in air, then placed in oven at 70 °C for several days (deposits made with pycnometer).
Hg^{203}	0.21	Hg^{++}	0.5g $Hg(NO_3)_2$/liter in ~0.01*N* HNO_3	10^{5}	Dried in atmosphere of H_2S (deposits made with pycnometer).

Three devices for depositing known amounts of radioactive solutions upon source mounts are the micropipet, the ultramicroburet, and the pycnometer (see fig. 5.2–1). Electrodeposition is also a widely used technique.

5.2.1. *Micropipets.* Micropipets are manipulated by rubber-bulb or syringe-type controls, the latter being desirable for pipet capacities under 200μl. Pipet capacities available are from 1 to 500μl. Micropipets should be calibrated "to contain" for more precise volumetric measurements. After delivery of a sample, the pipet must be rinsed out with carrier solution several times, and the rinses added

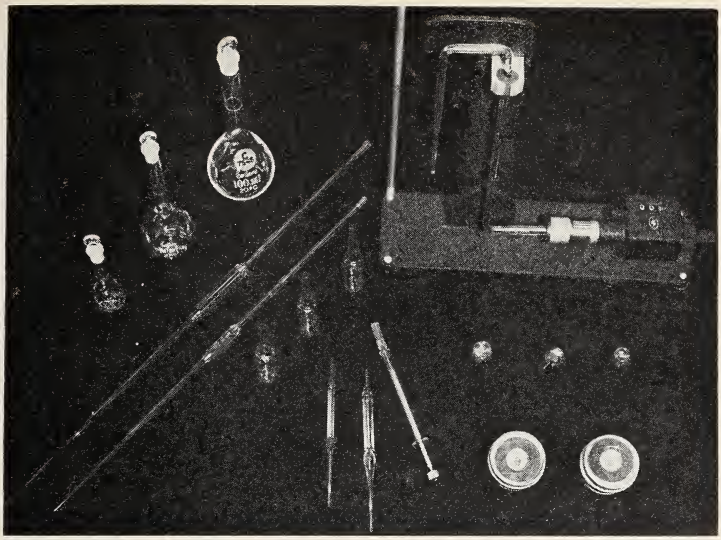


FIGURE 5.2–1. *Source-preparation paraphernalia.*
Top right, ultra-microburet. Bottom center, micropipet. Right middle, pycnometers. [Mann and Seliger, 1958a.]

to the source. It is claimed that, with careful attention, it is possible to make measurements reproducible to ± 0.1 percent.

5.2.2. *Mircoburet.* The microburet has a stainless-steel plunger which displaces mercury in a reservoir sealed off by a gasket contained in an aluminum bushing. The displaced mercury in turn forces exactly the same volume of the radioactive solution through a fine orifice. The volumes of liquid displaced are read on a micrometer dial, the calibration of which can be changed, from 10^{-3} to 10^{-4} ml per scale division, by using precision-ground plungers of different diameters. The microburet cannot be used for solutions such as those containing nitric acid or radioactive mercury. When solution concentrations are changed, the buret is flushed with several fillings of the solution to be used. It is common practice to use a different glass tip for each radionuclide. Sources can be prepared routinely with a precision of ± 0.1 percent.

5.2.3. *Pycnometer.* The pycnometer is to be preferred over the other two devices because a known mass is delivered in place of a known volume. The pycnometer arm is immersed below the surface of a solution and the bulb is gently heated

to remove air. When partially evacuated, the heat is removed and the solution enters the pycnometer. This process is repeated until the pycnometer is filled. By means of a fine wire, the filled pycnometer is suspended, arm down, from one of the stirrups of an analytical balance, and weighed. Aliquots can be removed from the pycnometer by very gently applying heat to the bulb (a small, heated, soldering iron held in proximity to the bulb will usually suffice). The accuracy of delivery is limited by the precision of the balance used.

5.2.4. *Electrodeposition.* Electrodeposition is applicable to the preparation of metal deposits. Many metals can be removed almost completely from solution by employing appropriate values of current density, *p*H, volume, composition of electrolyte, temperature, stirring speed and electrode material. Hudswell [1949] has prepared a comprehensive review of methods of source preparation and of references. The applicability of the methods of the treatment of radioactive materials has been outlined. Blanchard, Kahn, and Birkhoff [1960] have recently discussed the preparation of sources both by electro-deposition and adsorption.

5.3. Gas Samples

For the standardization of radioactive samples by counting in the gas phase, either in length-compensated internal gas counters or in ionization chambers, the radioactive nuclide must be converted to a suitable gas. This gas should be a good counting gas in itself or be compatible with a good counting gas such as methane, helium, or argon. The gas should be prepared by a reaction which yields this gas as the only product containing the radionuclide, and the reaction should be complete, in order to avoid isotope effects and the necessity of allowing for less than complete yields [Armstrong, Singer, Zbarsky, and Dunshee, 1950; Glasscock, 1954 and 1955a; Tolbert, 1956 and Brown, 1957]. Also, the gas should be chemically pure and especially free from contaminants which might have an adverse effect on the efficiency of the counter [Christman, Day, Hansell, and Anderson, 1955; Christman and Wolf, 1955; Christman, Stuber, and Bothner-by, 1956]. The gas should also not be adsorbed to an appreciable extent on the surfaces of the counters or other parts of the system.

Hydrogen-3 and carbon-14 are the radionuclides most frequently counted in the gas phase, although other radionuclides, particularly sulfur-35, can also be counted to advantage by this procedure. Carbon-14 can be counted as carbon dioxide which may be produced by the action of mineral acids on inorganic carbonates [Manov and Curtiss, 1951;

Mann, Seliger, Marlow, and Medlock, 1960], by the thermal decomposition of inorganic carbonates [Hawkings, Hunter, Mann, and Stevens, 1959], by wet combustion of organic samples [Van Slyde, Plazin, Weisiger, 1951; Christman, Day, Hansell, and Anderson, 1955], dry combustion of organic samples by Pregl's method [Glasscock, 1954 and 1955a] and by oxygen-bomb combustion [Marlow and Medlock, 1960].

For absolute counting, hydrogen-3 is counted as water vapor or tritium-hydrogen gas. Tritiated water vapor has, however, very bad adsorptive properties [Glasscock, 1955b]. A system has been reported [Merritt, 1958] to overcome this adsorption. Tritiated water is difficult to convert quantitatively to tritium-hydrogen [Glasscock, 1955a; Brown, 1957], but has been reduced with hot zinc [Rieck, Myers, and Palmer, 1956]. Merritt and Hawkings (1960) converted sulfur-35, in the form of barium sulfate, to sulfur dioxide by ignition with red phosphorus in an atmosphere of oxygen, and counted the sulfur dioxide, mixed with methane, in an internal gas counter in the proportional region.

5.4. Liquid Samples

5.4.1. *Formamide counting.* Samples for counting radioactive materials in solution in a $2\pi\beta$ windowless gas-flow counter are prepared by dissolving the radioactive material in an inert, low vapor-pressure organic solvent such as formamide [Schwebel, Isbell, and Karabinos, 1951; Schwebel and Moyer, 1954]. If the radioactive material is not readily soluble in the organic solvent used, it may first be dissolved in a liquid that is miscible with the organic solvent. A suitable aliquot of a solution of the radionuclide to be standardized is diluted from 10 to 100 times, depending upon the activity of the nuclide solution, with the organic solvent containing 1 percent of suitable carrier. This may be conveniently achieved, for example, by diluting 1 ml or ½ ml of the nuclide solution to 10 ml or 50 ml with the organic solvent, to give 10 to 100 times dilution, respectively. Up to 10 percent water content in the counting solution can be tolerated without change in the counting characteristics or efficiency of the internal gas counter. A sample of this counting solution, generally of 1 ml, is pipetted into a machined counting cell of specific dimensions and counted in the $2\pi\beta$ windowless gas-flow counter. If the dimensions of the counting cells used are always the same, and the same volume of solution is always counted, the depth of the solution is always the same. Therefore, not only will the geometry be constant in respect to the beta particles but any effects due to gamma rays will remain constant.

5.4.2. *Liquid scintillation counting.* Aqueous solutions may be incorporated in a water-alcohol-toluene solution for liquid scintillation counting in the ratio of 1:50:250, respectively. For organic compounds of hydrogen-3 and carbon-14, toluene is generally used as the solvent. Efficient liquid-scintillator combinations are 4 g/liter 2,5-diphenyloxazole (DPO), with 0.1 g/liter 1,4-di(2(5-phenyloxazole))-benzene (POPOP) in toluene and approximately 8 g/liter phenyl-biphenyloxadiazole (PBD) with 0.1 g/liter POPOP in toluene [Mann and Seliger, 1958a].

5.4.3. *Gel scintillation counting.* Carbon-14 has been assayed as barium carbonate in a gel medium by scintillation counting [Nathan, Davidson, Waggoner, and Berlin, 1958]. In this method the carbon-14-labeled barium carbonate is thoroughly dried at 200 °C, and finely ground. It is then mixed in a blender with toluene, a thixotropic gel, 2,5-diphenyloxazole, and 1,4-di(2,5-phenyloxazolyl) benzene. Samples are put in counting vials, well shaken, and stored in a deep-freeze unit until counted in a liquid scintillation spectrometer.

Part II. Measurement of Radioactivity for Clinical and Biological Purposes

6. Introduction

The use of radioactive materials other than radium and radon in the diagnosis and treatment of human disease and the investigation of biologic processes is a relatively new discipline. The materials, in general, did not exist until after the discovery of artificial radioactivity. Widespread use of them in large quantities is a phenomenon of the last 10 years. Instruments and techniques for the detection, identification, calibration, and measurement of these materials under diverse laboratory and clinical conditions have been developed, modified, discarded, and refined in great profusion. Until quite recently, the status of the field was too labile to allow of any recommendations even suggesting standardization or authenticity, and in some areas of the subject this is still the case. However, there are a considerable number of instruments and techniques which have stood the test of time sufficiently well to make it possible to evaluate their strengths and weaknesses, and to write at least general specifications for their proper construction and use.

The procedures of absolute standardization and even many of the methods of relative standardization suitable for use in standardizing laboratories are frequently of little value in the practical application of radionuclides to medical and biological problems. In such problems the measurements are usually of ratios of one radioactive sample to another. It is the purpose of this section of the manual to offer information concerning devices and procedures which can be used with reasonable confidence in specific situations. These data, together with the appendixes and references, should help newcomers in the field to choose proved and proper facilities and may assist the veteran worker to select such instruments and methods as will enable him to achieve results which are truly comparable with those of his colleagues.

It is not suggested or implied that these are the only methods and instruments applicable nor that there is no need for great improvements. The members of the Subcommittee believe, however, that those recommended in the following chapters have been proved to be reasonably satisfactory and that, at the time of writing, they are particularly to be recommended as standards when comparison with the work of others is desired.

The scope of this section has been limited to four major areas: Instrumentation and the preparation of reference standards; calibration and measurement prior to the use of the material; measurement of the radionuclide in the intact animal (human or otherwise); and measurement in aliquots or samples derived therefrom. Emphasis is placed upon basic principles and characteristics instead of specific designs and technical details, but wherever possible characteristic data of representative instruments have been included as a guide to the practical worker. These data must necessarily be obtained for each individual instrument by the worker himself, but it is anticipated that he will find the data presented here a useful check on his own measurements.

Discussion of specific clinical and biological applications of radionuclides has been avoided, except when necessary to illustrate the important principles of a method. In some of the more labile areas of the subject, for example section 10 on *in vivo* distribution studies, a broader discussion of the methods in use and some applications has been attempted, since specific recommendations seem undesirable at the present time.

Appendix A contains basic nuclear data on most of the radionuclides used in medical and biological work.

In the last three appendixes an attempt has been made to tabulate the recommended measurement procedures for the clinical uses of radionuclides. Appendix B includes much of the information in earlier tables in summary form and divides the types of measurement necessary into four classes: I. Preadministration measurement; II. *In vivo* measurement; III. Postadministration measurement; and IV. Ancillary measurements, such as disposal and monitoring procedures. In appendixes C and D are listed, respectively, the principal diagnostic and therapeutic procedures in regular use at the present time, and the type of measurement considered to be necessary for each. As already stated, it is not suggested that these are the only procedures or methods that can or should be used, but it is believed that the recommendations made will be of value to many clinical users, particularly those beginning new techniques.

7. Instruments Used in Relative Standardization

7.1. General

Relative standardization procedures inherently require calibration of an instrument in terms of a calibration standard and subsequent measurement of samples under conditions identical to those of calibration so that the comparison with the standard will be valid. Certain precautions must be observed with all standardizing instruments if accuracy is to be achieved.

The geometrical factors involved (for example, the distance from source to detector and the dimensions of the sample) must be maintained constant. The arrangement of scattering material in the vicinity of source and detector must be reproducible; for example, shielding used to protect the operator or equipment from stray radiation should not be moved since scattered radiation from the shielding may change both calibration and background. Where completely fixed conditions cannot be achieved (for example, with unavoidable variations in sample size), corrections should be made from data obtained by previous investigation of the pertinent parameters.

Calibration of measuring systems is accomplished with relative standards available commercially or from a national standardizing laboratory. A list of the standards available at this time is given in the Isotope Index. In addition, samples may be sent to the U.S. National Bureau of Standards and the Canadian National Research Council for calibration. The equipment employed should be tested

periodically with calibration or performance standards (see sec. 1.1). The use of these standards is discussed in section 7.7. The type of testing required and its frequency will depend on the equipment employed. Testing may involve the observation of the voltage across the counting chamber, the determination of the plateau characteristics of a counter, background evaluation, and the response of the equipment to the standard. If pulse-height analyzers or discriminators are employed, the energy response should be tested. Experience will generally determine the necessary frequency of testing but, in the case of counters, the operating conditions, the response to the standard, and the background should be checked at least once a day.

The contribution of the background must always be carefully considered, and if large or variable or both, frequent background determinations may be necessary in order to achieve the desired accuracy (see sec. 2.5).

In selecting a standardization procedure the accuracy required in the ultimate use of the radioactive material should be considered. To endeavor to achieve 1-percent precision in the measurement of a sample when 5 percent will suffice is usually pointless and very time consuming.

The physical characteristics of many radionuclides important in biology and medicine are listed in appendix A. These characteristics determine the selection of appropriate standardization methods and instruments.

In the sections immediately following, the principal calibration instruments are briefly described, especially with regard to their advantages and disadvantages. References to more detailed descriptions are cited. Characteristic data for various instruments are summarized in tables 7.1–1. and 7.1–2. for representative gamma- and beta-emitting radionuclides. Approximate estimates of the response of these instruments to other radionuclides may be estimated from a consideration of appendix A with tables 7.1–1. and 7.1–2.

7.2. Ionization-Current-Measuring Systems

The ionization system may consist of an ionization chamber and a device for measuring the current. These components may be permanently connected together as one unit or they may be separable. The theory of operation of ionization chambers has been described in section 2.1. The types which have been employed are so numerous as to preclude any complete description here. The characteristics of some chambers and measuring systems are tabulated in table

TABLE 7.1–1. *Typical characteristics of radionuclide measuring equipment for γ-ray samples with some typical observations*

Type of equipment	Chamber, tube or crystal	Background or other limitation	Volume of sample used	Distance range [1]	Response				Approximate useful range [2]
					I^{131}	Co^{60}	Ra	P^{32} *	
Lauritsen electroscope.[7]	Cylinder 7.5 cm. x 5.5 cm (diam.) Al.	0.002 div/sec.	Variable (small).	25–100 cm	0.193 div/sec/mc.	1.14 div/sec/mc.	0.73 div/sec/mc.	0.0066 div/sec/mc.	0.01 mc–100 mc I^{131}.[2a]
Chalk River electroscope.[3]	Spherical chamber	BEA radium ~2.47 μc.	5 ml sample.	Jig—1 cm away.	1.20 div/sec/mc.	7.95 div/sec/mc.	5.06 div/sec/mc.		
NBS 4πγ ionization chamber and Lindemann Ryerson electrometer.[3]	Cylinder 10″ diam. x 12″ long.	BEA radium ~0.125 μc.	5 ml sample.	Fixed	34.2 μμa/mc.	151.0 μμa/mc.	109. 5 μμa/mc.		1 μgm–300 μgm radium.
Ionization chamber+d-c amplifier.[4]	Cylinder 2.00 x 2.00 cm carbon.	Noise.	Variable (small).	10–100 cm	27.4 mm/mc.	153 mm/mc.	100 mm/mg.		0.02 mc–1000 mc I^{131}.[2a]
NPL well chamber+current measuring device.[5]	Cylinder 17.0 cm x 17.0 cm well 6.6 cm diam. x 12.5 cm.	Noise.	3 cc up to about 100 cc.	Fixed	11 μμa/mc	53 μμa/mc	34 μμa/mc	0.078 μμa/mc.	1 μc–several 100 mc I^{131}.[2a]
Braestrup well chamber+victorcen.[6]	Cylinder	Leakage very low.	5 cc	Fixed	9.5 div/min/mc.		26.8 div/min/mg.	0.15 div/min/mc.	0.03 mc–to 7 mc I^{131}.[2a]
GM tube for γ rays.[6]	TGC–8 copper wall (end-window type).	30 c/min	Variable small.	20–100 cm	7 c/min/μc.	55 c/min/μc.	32 c/min/μg.		5 μc–2 mc I^{131}. [2b]
GM tube ring for γ rays.[9]	6 tubes 26 cm long, lead cathode.	1000 c/min	2,000 ml	Fixed	7.2×10^3 c/min/μc.	1×10^4 c/min/μc.		60 c/min/μc.	0.1 μc–4 μc I^{131}, [2b]

Scintillation crystal+scaler.[7]	NaI 1¾″ x 2″.	Without PHA.	1350 c/min	1,000 ml	Sample on top.	1.95×10^4 c/min/μc.	2.86×10^4 c/min/μc.		45.6 c/min/μc.	0.07 μc–30μc I^{131}, 2c
		With PHA.	20–80 c/min.			6.13×10^3 c/min/μc.	3.66×10^3 c/min/μc.			0.013 μc–30 μc I^{131}.
Well-type crystal+scaler.[8]	NaI 1¾″ x 2″ hole ¾″ x 1½″.	Without PHA.	150 c/min	4 ml	Fixed (in well).	8.45×10^5 c/min/μc.	9.1×10^5 c/min/μc.		1.32×10^4 c/min/μc.	2×10^{-4} μc—0.7 μc I^{131}, 2c
		With PHA.	5–20 c/min			5.08×10^5 c/min/μc.	1.82×10^5 c/min/μc.			3.7×10^{-5}μc—1.2 μc I^{131}.

[1] The responses quoted are for the shorter of these distances. In all measurements where appreciable distance is used, it is assumed that scattering effects are reduced to a minimum.

[2] In most cases, the lower limit of the range has been taken as the activity equal to the background equivalent activity.

The upper limit (a) in ionization chambers, is usually not sharply defined and may be limited by saturation considerations, range of amplifier, or simply protection of the operator during the measurement;
(b) in Geiger-Müller counters, is taken as 30,000 c/min, at which level a 5% dead-time correction would be necessary for a dead time of 100 μsec;
(c) in scintillation counters, is taken as 600,000 c/min at which level a 5% dead-time correction would be necessary for a dead time of 5 μsec.

[3] Data from National Bureau of Standards.

[4] Data from Sinclair, Trott and Belcher (1954).

[5] Data from NBS, NRC, and the University of Texas, M. D. Anderson Hospital and Tumor Institute in agreement.

[6] Data from J. Hale, University of Pennsylvania.

[7] Data from Physics Department, University of Texas, M. D. Anderson Hospital and Tumor Institute.

[8] Data from University of Texas and University of Pennsylvania in agreement.

[9] Data from Veall and Vetter (1952).

* *Bremsstrahlung*.

TABLE 7.1–2. *Typical characteristics of radionuclide measuring equipment for β-particle samples, with some typical observations*

Type of equipment	Chamber, tube or scintillator	Background or other limitation	Type of sample	Geometry	Response		Approximate range
					C-14	P-32	
Chalk River electroscope (TQQ)	----------	0.0003 div/sec----	Evaporated sample on planchette.	2π----------	----------	0.45 div/sec/μc---	0.001 μc–100 μc
NPL well chamber+d-c amplifier.	Cylinder window in base.	Noise, amplifier, etc.	Liquid, 1 ml in cup.	Cup under window.	----------	265 $\mu\mu$a/mc------	0, 05μc–25μc [1a]
End-window GM counter-	Window 1.4 mg/cm^2 2.3 mg/cm^2.	20 c/min---------	Evaporated layer on planchette.	Sample under window.	2.4×10^4 c/min/μc-	4.4×10^5 c/min/μc	7×10^{-5} μc–0.07 μc [1b]
Gas-flow counter--------	0.12 mg/cm^2-----	3 to 50 c/min----	Evaporated sample on planchette.	Inside counter---	6.1×10^4 c/min/μc-	11×10^5 c/min/μc-	3×10^{-5} μc–0.03 μc [1b]
"Liquid" GM counter (test tube type).	Jacketed test tube, wall 30 mg/cm^2.	10 c/min---------	Liquid 10 ml----	Fixed----------	----------	2.2×10^5 c/min/μc.	4×10^{-5} μc–0.14 μc [1b]
Liquid scintillation counter.	----------	40 c/min---------	Liquid----------	Fixed----------	7.3×10^5 c/min/μc	----------	6×10^{-5} –0.04 μc [1c]

[1] In most cases, the lower limit of the range has been taken as the activity equal to the background equivalent activity.
The upper limit (a) in ionization chambers, is usually not sharply defined and may be limited by saturation considerations, range of amplifier, or simply protection of the operator during the measurement;
(b) in Geiger counters, is taken as 30,000 c/min, at which level a 5% dead-time correction would be necessary for a dead time of 100 μsec;
(c) in scintillation counters, is taken as 600,000 c/min at which level a 5% dead-time correction would be necessary for a dead time of 5 μsec.

7.1–1. For more complete information, the reader is referred to the literature [Rossi and Staub, 1949; Wilkinson, 1950].

With all ionization-current-measuring systems, good electrical insulation is necessary. Dirt across insulators will render an instrument unreliable. With a self-contained instrument, such as an electroscope, the danger of the insulators becoming dirty is less than with the separate ionization chamber and detector systems described in section 7.2.2. The insulation should be tested periodically by charging the fiber with no source present and observing the leakage rate (which will include background) (table 7.1–1).

The principal advantages of ionization systems are their accuracy, reliability, and large activity range; however their sensitivity is generally less than that of counting systems.

7.2.1. *Electroscopes.* The principal advantages of electroscopes are simplicity, ease of operation, reliability, and low cost [Harnwell and Livingood, 1933; Strong, 1943]. The disadvantages are their relatively short linear scale and small range of drift rates. They are generally used for gamma-ray samples but some models may also be used for beta-ray sources [Mann and Seliger, 1958a].

7.2.2. *Electrometers.* Two principal types of electrometers are the quartz-fiber and vacuum-tube electrometers. The fiber type is simple and robust but generally of smaller range than the vacuum-tube instrument.

Two fiber electrometers are commonly used; the string and the quadrant. Numerous variations of each exist [Harnwell and Livingood, 1933; Strong, 1943]. Sensitivities as great as 5×10^{-15} coulomb per scale division are obtainable.

Vacuum-tube electrometers with multiple current ranges, high maximum gain, and low zero drift are available. Inverse feedback d–c amplifiers which will detect 10^{-15} ampere and have a wide range are not uncommon. The most sensitive electrometer presently available is the vibrating-reed type, which can detect currents as low as 10^{-17} ampere under special conditions. An added advantage of electronic systems is that strip chart recorders can easily be used to produce a permanent record.

Various kinds of measuring circuit may be used. In the rate-of-drift method [Dubridge and Brown, 1933], the output reading is linearly proportional to the radiation flux passing through the chamber. In the null method of Townsend, the change in voltage produced across a capacitor by the ionization current is counterbalanced by an equal and opposite voltage supplied from a potentiometer. This may be accomplished automatically [Garfinkel, 1959].

7.2.3. *Types of ionization chamber.* Almost any ionization chamber can be employed for secondary standardization of gamma-emitting nuclides. An air-equivalent-wall chamber is particularly useful when gamma-ray exposure-dose rates are the primary information required. However, for routine calibration of sample activity it is preferable to use a chamber especially designed for this purpose (sec. 8.2).

The reentrant or well chamber is designed so that the sample is surrounded by the sensitive volume of the ionization chamber (fig. 7.2–1). This provides an arrangement of high sensitivity on which sample position and volume, within limits, have relatively little influence. A further advantage is that such a chamber may be easily shielded so that back-

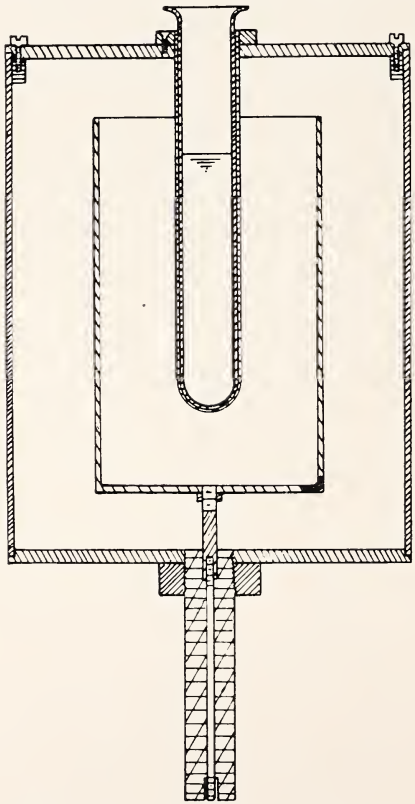


FIGURE 7.2–1. *Well-type ionization chamber designed by C. B. Braestrup for the assay of gamma-emitting nuclides.*

[Feitelberg, 1949; reprinted from Science by permission of the American Association for the Advancement of Science.]

TABLE 7.2–1. *NPL β-γ well-type ionization chamber*

(A) γ-ray chamber

Radionuclide	r/mc-h at 1 cm	Form of sample	Background equivalent activity μc	Response μμa/mc	Source of data
Iodine-131	2.18	5 ml	0.945	10.6	NBS
Gold-198	2.35	do	0.929	10.9	NBS
Radium-226, 0.5 mm Pt filter.	8.25	Ra source 3 mm long in Pt tube 6 mm long.	0.290	34.5	NPL
Cobalt-60	12.8	5 ml	0.188	53.3	NBS
Sodium-24	18.4	do	0.133	75.2	NBS

(B) β-ray chamber

Radionuclide	$\bar{E}_\beta$ (Mev)	Form of sample	Background equivalent activity μc	Response μμa/mc	Source of data
Phosphorus-32	0.69	1 ml solution in polyethylene dish.	0.037	268	NPL
Iodine-131	0.187	do	0.137	73	NPL
Gold-198	0.331	do	0.073	137	NPL
Thallium-204	0.24	do	0.159	62.8	NRC
Promethium-147	0.061	do	1.43	7.02	NRC
$Sr^{90}+Y^{90}$	0.20+0.93	do	0.024	419 ($Sr^{90}+Y^{90}$)	NRC
Y^{90}	0.93	do	0.030	335 (Y^{90})	NPL

ground radiation effects are small (for low activities) and protection is provided for the operator (for high activities).

Ionization chambers employing essentially 2π geometry have been used to standardize radionuclides which emit beta rays only; for example, the Chalk River Electroscope (table 7.1–2).

An ionization instrument which combines the well gamma-ray and 2π beta-particle chambers [Hine and Brownell, 1956, ch. 11, p. 527, "Standardization of X-Ray Beams and Radioactive Isotopes," by W. K. Sinclair] has been further developed by the National Physical Laboratory [Perry, Dale, and Pulfer, 1956] (figs. 7.2–2 and 7.2–3.) The lower half of the gamma-ray chamber is used as the beta-ray chamber which has a thin window to admit beta particles and to avoid a humid atmosphere around the insulators. Some typical results of measurements made with such combined $\beta-\gamma$ ionization chambers, developed by the National Physical Laboratory, are shown in tables 7.2–1.

7.3. Counting Systems

Counting systems are more sensitive than ionization chambers but are also less stable. They must therefore be

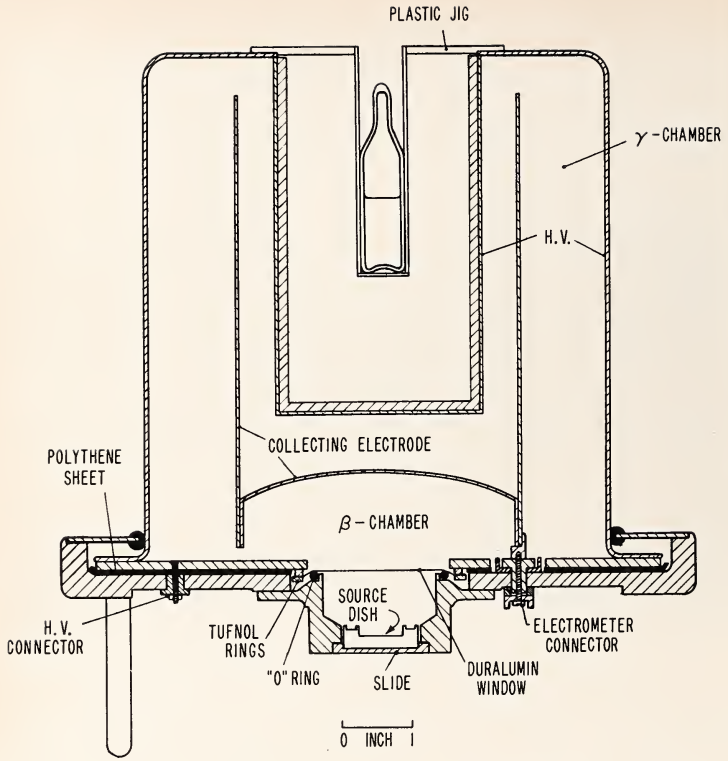


FIGURE 7.2–2. *Combined beta-gamma reference ionization chamber.* [Courtesy of the National Physical Laboratory.]

tested more often with performance or reference standards (sec. 7.7) to ensure satisfactory results.

When low activity samples are measured, correction for background count rate must be made. Random fluctuations in counting rate necessitate consideration of statistical factors (sec. 2.5.1) [Hine and Brownell, 1956, ch. 5, "Geiger-Müller Counters and Proportional Counters," by W. K. Sinclair]. At low counting rates, long counting times may be necessary to achieve statistical accuracy. In these circumstances it is important to choose the disposition of time between counting sample and background and background alone so that the greatest precision will be achieved in the time available (see sec. 2.5.2). When high activity samples are assayed, correction for loss of counts may have

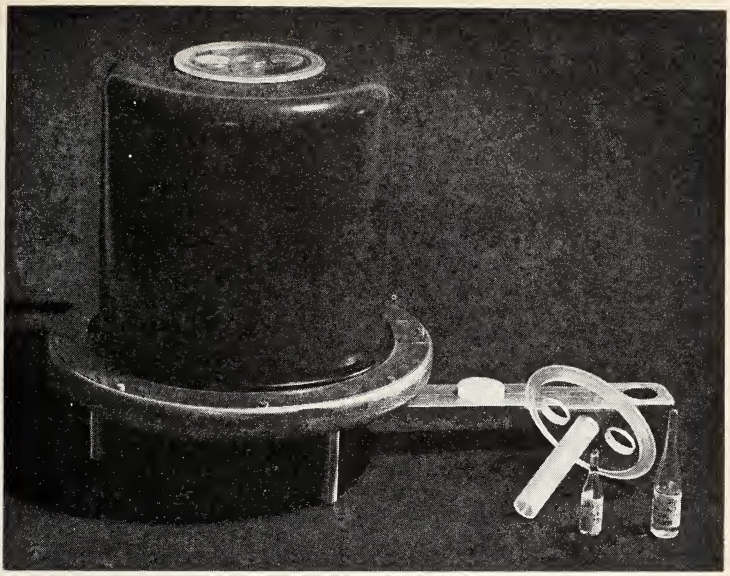


FIGURE 7.2–3. *Combined beta-gamma reference ionization chamber with plastic jig for the support of small ampoules.*

[Courtesy of the National Physical Laboratory.]

to be made due to finite resolution time or dead time of the system (see sec. 2.5.5).

Counters require auxiliary electronic equipment including high voltage supply, amplifier, scaler and count-registering unit. Count-rate meters may also be used. The required stability of the high-voltage supply, and the required sensitivity and linearity of the amplifier, are dictated by both the detector used and the application. (For a detailed discussion, see, for example, Elmore and Sands, 1949, and Price, 1958.)

The amplitude of electrical pulses produced by proportional and scintillation counters is proportional to the energy delivered to the detector by each primary ionizing event. In certain applications this proportionality is useful. For example, a simple discriminator may be used to eliminate pulses below a certain amplitude (thus, for example, excluding scattered radiation); or a pulse-height analyzer may be used to select, electronically, pulses which exceed a height determined by one adjustment (baseline) but do not exceed this height by more than an amount determined by another control (channel width or "window"). Equipment is also

available to measure an entire pulse-height spectrum by continuously changing the baseline control while plotting the counting rate on a strip chart recorder. Multichannel analyzers can achieve this result more quickly and effectively by simultaneously sorting and recording pulses of various heights. The precise calibration of equipment which includes a pulse-height analyzer is complex. Among the most important factors to be considered are the following: The amplifier should be linear and nonoverloading; the baseline calibration should be tested for drift; the channel width should be checked as a function of baseline setting and the overall performance should be tested as a function of counting rate.

If the quantity of interest is the variation of the counting rate with time, a count-rate meter and pen recorder or a scaler and a digital printer may be used.

Circuitry used for counting work is discussed by Elmore and Sands [1949] and Price [1958].

7.4. Geiger-Müller Counters

The principal advantage of the Geiger-Müller counter lies in the simplicity of its necessary associated circuitry. The sensitivity for beta particles is excellent but for gamma rays the sensitivity is less than that of the scintillation counter.

Many special Geiger-Müller counters have been produced. For example: thin-window Geiger-Müller tubes are available for beta-particle measurements, while special cathode materials such as bismuth can increase the sensitivity to gamma rays.

Special Geiger-Müller counter equipment is available also for measuring low-energy beta particles. An example of such special equipment is the windowless 2π flow counter in which the samples are placed inside the counting chamber, through which the counting gas flows; the overall efficiency, including backscatter, may exceed 50 percent. External counting may be accomplished with very thin-wall or "micro-mil" window counters. Libby (1957) has developed a Geiger-Müller counter of this type in which the sample is wrapped around the counter, enabling a large area of sample to be counted.

7.5. Proportional Counters

Proportional counters have a shorter dead time and often a longer and flatter plateau than Geiger-Müller tubes, but the techniques of counting are more elaborate. They may be

used for all of the same purposes as Geiger-Müller counters. In addition, they are very useful for counting at high counting rates and also for alpha-particle counting, as in this application the beta particles can be discriminated against. The flow proportional counter for internal solid [Heintze and Fischbeck, 1957; Verly, Bricteux-Grégoire, Koch, and Dewey, 1958] or liquid (organic solvent) [Schwebel, Isbell, and Karabinos, 1951; Schwebel, Isbell, and Moyer, 1954] sources is very similar to the flow-type Geiger-Müller counter and some types are available which may be used either for Geiger-Müller or proportional counting. Overall efficiencies may be as high as 80 percent when backscattering is pronounced.

7.6. Scintillation Counters

The scintillation counter is probably the most useful instrument for the assay of low-activity gamma-ray samples since it is more efficient for this purpose than are the Geiger-Müller or proportional counters.

When feasible, gamma-ray counting of samples is usually preferred to other methods because of the relative freedom from absorption and self-absorption corrections and special preparation procedures which are often necessary in beta-particle sample counting.

Many different luminescent materials have been found useful for scintillation counting and these may be either inorganic or organic in composition and either solid or liquid in phase. Liquid scintillators are especially useful when the radioactive material can be dissolved in the luminescent medium (see sec. 12.5.4). Solid organic phosphors such as anthracene and stilbene have been widely used for spectral analysis studies of beta-particle emitters, and their efficiency for beta-particle detection is similar to that of a thin-window Geiger-Müller tube. These crystals are less efficient for gamma-ray detection than the solid inorganic crystals, but are nevertheless useful in gamma-ray dose-rate studies because their energy absorption is similar to that of tissue.

Solid inorganic crystals are most widely used for gamma-ray sample counting techniques. Thallium-activated sodium iodide is the most commonly used crystal for the assay of gamma emitters and the *bremsstrahlung* from high-energy beta emitters. Single crystals, usually in the form of cylinders, are available in a variety of sizes ranging up to several inches in diameter and in depth. For high-efficiency counting of low-level gamma-ray or *bremsstrahlung* sources such a crystal with a well is commonly used. Sodium iodide has a larger photoelectric cross section than most other

suitable crystals and is therefore more efficient for gamma-ray assay. Furthermore the amplitude of the light pulse produced per unit-energy absorption is high (see sec. 2.4).

The true advantage of a scintillation counter over a Geiger-Müller counter is not as great as a comparison of efficiencies alone may indicate, because background counting rate in a scintillation detector is usually higher (even if heavy shielding is used). Comparison may better be made on the basis of minimum detectable activity which is discussed in section 2.5.3. The short-term stability of a scintillation counter is possibly no better than that of a Geiger-Müller counter, so that frequent calibration is required. A performance standard, while useful with a scintillation counter, should be employed cautiously because changes in the detection system affect its energy response unpredictably.

Scintillation detectors and proportional counters usually involve the use of more complicated electronic equipment than do Geiger-Müller counters and the requirements for stability of the high-voltage supply are more critical and more amplification of the pulse is needed.

Two recent reports [Ross, 1959; Harris, Hamblen, and Francis, 1959] deal with the medical applications of scintillation counting.

7.6.1. *Application of scintillation counting.* Scintillation counters are particularly useful in the following applications:

(a) Highly collimated and shielded arrangements, which are movable, for *in vivo* measurement.

(b) Crystal and source in a fixed geometry relation for sample counting, either

1. with the source at a distance from the crystal (for example, in the measurement of beta particles in the defined solid angle method, or in the measurement of gamma rays from bulk samples), or

2. with the source inserted inside the crystal volume, in the well-type crystal, or surrounding the crystal volume on most of its faces.

In each case both the source and detector are surrounded by stationary shielding.

7.6.2. *Well-type scintillation counter.* The well-type scintillation counter is the most useful type for routine measurements of low-activity gamma-ray samples (fig. 7.6–1). A typical model uses a sodium iodide (thallium-activated) crystal 1¾ in. in diameter and 2 in. high, in which the well is a cavity ¾ in. in diameter which extends 1½ in. into the crystal. The crystal is contained in an aluminum shell with a glass window and is mounted directly on the face of the

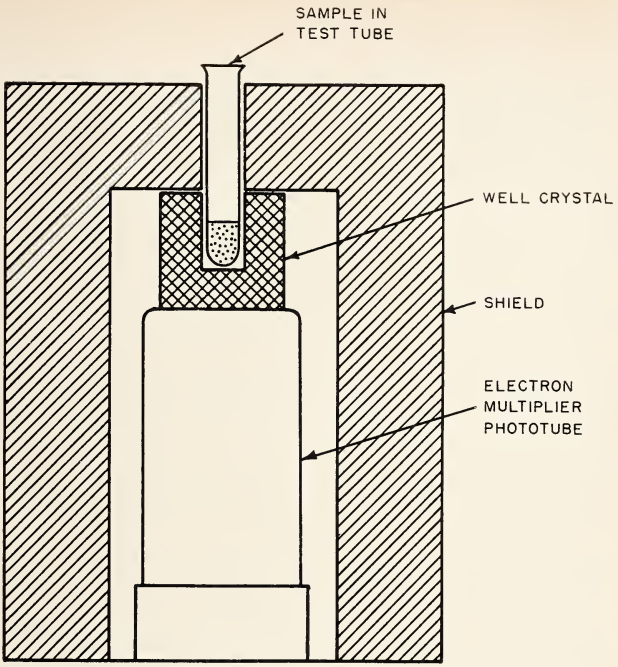


FIGURE 7.6–1. *Well crystal counter.*

electron-multiplier phototube. The whole assembly is surrounded by lead shielding. Optimum ratios of sample-to-background counts are obtained by varying the discriminator and high-voltage levels. Pulse-height-analysis methods may also be used.

The efficiencies and response of typical systems of this kind for several radionuclides are given in tables 7.6–1. and 7.6–2.

7.6.3. *Liquid scintillation counter.* The liquid scintillation counter has recently come into rather general use for the relative assay of hydrogen-3 (tritium) and carbon-14, particularly when these are used as tracers in biological experiments. The low energies of hydrogen-3 and carbon-14 beta particles require, for reasonable counting efficiencies, a source-preparation technique which introduces a minimum of source self-absorption. Gaseous samples could be counted as H_2^3 or $C^{14}O_2$ in an internal gas counter but, for the routine analysis of large numbers of samples, it is very much simpler

TABLE 7.6–1. *Well scintillation counter—no pulse-height analyzer* [a]

4.0-ml samples [b]

Radionuclide	Efficiency in %	Response in c/min/μc	Background in c/min	Background equivalent activity in μc	Upper limit [c] in μc
Chromium-51	4.95	1.08×10^{5}	200	1.85×10^{-3}	5.55
Iodine-131	41.0	9.10×10^{5}	200	2.20×10^{-4}	0.66
Gold-198	41.3	9.18×10^{5}	200	2.18×10^{-4}	0.65
Iron-59	26.0	5.77×10^{5}	200	3.47×10^{-4}	1.04
Cobalt-60	43.3	9.61×10^{5}	200	2.08×10^{-4}	0.625
Phosphorus-32 *bremsstrahlung* (833 mg/cm² absorber, glass + Al)	1.0	2.22×10^{4}	200	9.02×10^{-3}	27.0

[a] With a sodium iodide crystal 2″×1¾″, well ¾″ diameter ×1½″ deep, with discriminator setting just above noise level.

[b] The response for different volumes must be measured in each individual apparatus with each type of container. In this instrument the variation is about −3.5%/ml for I-131 and Au-198 and −1.5%/ml for Fe-59 and Co-60.

[c] Based on activity producing counting rate of 600,000 c/min which would have 5% dead-time loss for a dead time of 5 μsec.

Data from Physics Department, The University of Texas, M. D. Anderson Hospital and Tumor Institute. These are representative data only and different results must be expected if different instrument settings are used.

TABLE 7.6–2. *Well scintillation counter with pulse-height analyzer* [a]

4.0-ml samples [b]

Radionuclide	Baseline volts	Window volts	Efficiency in %	Response in c/min/μc	Background in c/min	Background equivalent activity in μc	Upper limit [c] in μc
Chromium-51	12.0	6.0	3.1	6.9×10^{4}	19	28.0×10^{-5}	8.7
Iodine-131	15.0	6.0	23.0	5.08×10^{5}	19	3.7×10^{-5}	1.2
Gold-198	16.5	6.0	16.4	3.64×10^{5}	19	5.2×10^{-5}	1.6
Iron-59	49.0	[d] 8.0	4.7	1.03×10^{5}	7	6.8×10^{-5}	5.8
Cobalt-60	55.0	[d] 8.0	8.3	1.82×10^{5}	7	3.8×10^{-5}	3.3

[a] With a sodium iodide crystal 2″×1¾″, well ¾″ diameter ×1½″ deep, and single channel pulse-height analyzer set on photopeak.

[b] The response for different volumes must be measured in each individual apparatus with each type of container. In this instrument the variation is about −3.5%/ml for I-131 and Au-198 and −1.5%/ml for Fe-59 and Co-60.

[c] Based on activity producing counting rate of 600,000 c/min which would have 5% dead time for loss for a dead time of 5 μsec.

[d] Not calibrated in volts—actually more than 8.0 volts.

Data from Physics Department, The University of Texas, M. D. Anderson Hospital and Tumor Institute. These are representative data only and different results must be expected if different instrument settings are used.

to introduce aqueous samples into the liquid scintillator solution. Further, the linear response of the liquid scintillator to energy absorbed permits discrimination between hydrogen-3 and carbon-14 by means of pulse-height analysis, which is important in double labeling experiments.

Phototube, amplifier and high-voltage requirements are similar to those for ordinary solid scintillation counting. Usually, higher amplification (20,000 to 50,000) is required since the amplitude of the pulses produced is low. Operation at lower temperatures (about 0 °C) in a refrigerator and the use of coincidence techniques where two phototubes view the same sample effect a large increase in signal-to-noise ratio. Due to the complexity of setting up a liquid-scintillation-counting unit, it is suggested that commercially available units be used for routine counting requirements. Tritiated-water and carbon-14-benzoic-acid or barium carbonate standards are presently available and can be added to unknown samples as "spikes," for determining counting efficiencies and in addition for the setting of discrimination levels in those cases where hydrogen-3 and carbon-14 are used in the same sample.

Water samples are usually dissolved in alcohol and then in toluene which contains the phosphor. A water:alcohol:-toluene ratio of 1:50:250 has been found to give extremely reproducible results. In those cases where the lower acitivities are to be measured, large volumes of water are necessary, and dioxane may be used in place of toluene. Dioxane will result in smaller pulse heights than toluene at optimum solute concentrations; however, the larger tolerance for water can more than compensate for this. (For more specific details, the reader is referred to Davidson and Feigelson, 1957; Bell and Hayes, 1958; and Mann and Seliger, 1958a.)

7.7. The Use of Standards and Reference Sources

Standards are used either for calibration or for testing a measuring system. Since all detecting systems are subject to faults, frequent checks with some type of standard are necessary to ensure that difficulties are discovered. A routine program of testing should be followed. Although in many applications only relative results between a group of samples are required and an aliquot of the original sample is used for comparison purposes, it is still desirable to use a performance standard to test equipment behavior.

7.7.1. *"Performance" standards.* "Performance" standards are commonly used for testing the constancy of response of instruments. Performance standards do not test all aspects of the response of a measuring system for some other radionuclide, because the energies of the radiations emitted are not usually the same. The standard should be permanently mounted in a container similar to the sample-holding containers. Because of its extremely long half-life, radium-

226 in equilibrium with its decay products, is a frequent choice for a gamma-ray standard, although both cobalt-60 and cesium-barium-137 are used. Cesium-barium-137 is particularly useful as a performance standard for gamma-ray spectrometers because of its single 0.662-Mev line. Beta-particle performance standards include radium-226 [Mann and Seliger, 1958a], radium D+E and strontium-yttrium-90. Corrections for decay must be made when the standard is used over a period of years. Uncertainty as to the half-life of radium D+E reduces its usefulness as a performance standard.

7.7.2. *Calibration standards.* Calibration standards usually cannot be maintained for long periods, since many radionuclides of interest have short half-lives. Standards of various short-lived radionuclides are available (see, e.g., the Isotope Index) and secondary standardizing equipment should be calibrated periodically.

7.7.3. *Simulated standards.* Simulated standards attempt to achieve the advantages of both calibration and performance standards for short-lived radionuclides. Iodine-131 may be simulated by a mixture of barium-133 and cesium-barium-137 which is useful for about 10 years [Brucer, Oddie, and Eldridge, 1956]. Such simulated standards only approximate the radiation characteristics of the actual radionuclide (although perhaps closely) and changes with time due to the differences in half-lives among the constituents must be corrected for. The decay of such mixtures is not exponential and special charts must be used. They are not suitable for the calibration of scintillation spectrometers.

8. Preadministration Sample Measurement

8.1. General

Shipments of radioactive nuclides received by institutions fall into two general categories: small quantities (less than 1 mc) to be used directly for diagnostic tests and tracer metabolic studies; or large quantities (more than 1 mc) to be used either directly for therapy or, after dilution, for the preparation of aliquots for either therapy or tracer doses. Currently, commercial suppliers of radioactive materials provide quantities that are usually reliably calibrated. Nevertheless, the final responsibility for the accuracy of the amount administered to a patient rests with the user and each shipment or aliquot used should be tested.

Regardless of any previous assay of the stock solution, individual doses should be checked to ensure the accuracy of dispensing.

Specifications for instruments suitable for this type of assay and procedures for their use are [after Sinclair, 1951]:

1. The instrument should be such that it can be calibrated with a standard sample of each radionuclide for which it is used, and the instrument behavior should be checked thereafter with a performance standard.

2. The geometrical conditions of measurement should be quickly and accurately reproducible.

3. The measurements should take only a short time to perform, and the reading should be easily translated into units of activity.

4. A precision of about 2 percent should be possible, and the range of the instrument should be wide.

5. The shielding should be adequate to protect the operator, for the highest activity to be measured, and should be permanent.

Although several of the general classes of instruments described in section 7 may be used, ionization-current-measuring instruments usually best fulfill the specifications above [Feitelberg, 1949].

8.2. Radioactivity Assay Methods

8.2.1. *Methods of calibration.* Measuring instruments can be calibrated for most clinically used radioactive material by means of calibration standards obtainable from commercial suppliers or from national standardizing laboratories (see The Isotope Index). Calibration standards are ordinarily of low activity (a few microcuries) and can usually be used directly for the calibration of counting equipment. Many ionization chambers, however, may not be sufficiently sensitive to make direct measurements of a calibration standard. For initial calibration therefore, an aliquot of a total shipment must be used as an intermediate step for comparison with the calibration standard. In many cases dilution of the aliquot may be necessary and the comparison then has to be made by counting techniques.

8.2.2. *Millicurie amounts of gamma- or high-energy beta-emitting radionuclides.*

8.2.21. *Well-ionization-chamber measuring methods* (sec. 7.2.3). The well-ionization chamber is a particularly useful method for the direct assay of shipments of radioactive materials of high activity, and with suitable electrometers may cover a wide activity range. The chamber may be designed to accept standard-sized shipping bottles [Sinclair and Newberry, 1951]. Variation of sample-bottle size and type may cause variations in assay values due to changes in geometry, sample self-absorption and container absorption,

which may require small corrections. A modification of the gamma-ray instrument enables beta-ray measurements to be made by including a window to a beta-ray sample chamber [Hine and Brownell, 1956; ch. 11, p. 527, "Standardization of X-Ray Beams and Radioactive Isotopes," by W. K. Sinclair; Perry, Dale, and Pulfer, 1956] (see also sec. 7.2.3). Another type of well-ionization chamber has been designed by Braestrup to be used with a standard X-ray electrometer [Feitelberg, 1959] and is most useful for assaying solutions of the order of 1 mc/ml. The well is the proper size and shape to accept standard laboratory test tubes. Data pertaining to the NPL chamber and the Braestrup chamber, both of which are commercially available, are included in tables 7.1–1 and 7.2–1.

Either of these instruments can be used to assay samples of radionuclides that emit high-energy beta particles, by measuring the ionization produced by *bremsstrahlung* from the walls of the chamber and within the solution [Alper and du Preez, 1949]. These measurements should be made with standard containers and volumes.

8.2.22. *Measuring methods with the sample at a distance.* An alternative method for routine assay is that in which the ionization produced by gamma rays from a radioactive sample is measured by an ionization chamber located at a distance from the source. The method is widely used and its principles are discussed in section 3.6. The technique and applications of the method are described by Sinclair, Trott, and Belcher [1954]. The geometry is conveniently controlled by the use of an optical bench. The useful range of measurement of the instrument can be extended by varying the distance and then applying the inverse square law. In this case the measuring distance should be several times greater than the linear dimensions of the sample and chamber in order to minimize the error arising from uncertainty in effective distance between source and detector (often 50 to 100 cm). An adequate distance should be maintained between any scattering material and both source and detector in order to minimize the amount of scattered radiation entering the detector.

If the ionization chamber is "air equivalent" for the energy of the gamma rays being measured, known values of the specific gamma-ray emission constant for the radionuclide (r per mc-hr at 1 meter) (app. A) may be used to determine the activity of the sample directly. However, corrections for self-absorption in the radioactive material and for absorption in the container wall must be applied (see also sec. 3.6.1).

If the ionization chamber is not air equivalent, it must be calibrated with a standard of the radionuclide in question. The ionization chamber may be heavily shielded (several mm of lead) to discriminate against scattered radiation.

8.2.3. *Microcurie amounts of gamma- and high-energy beta-emitting nuclides.* Microcurie amounts are normally used in tracer or diagnostic studies. In these studies the measurements are almost always expressed as percentages of the administered amount and, consequently, the assay is less important than when these materials are used therapeutically. In such tracer applications, all measurements are precisely related to the activity of an aliquot of the radionuclide sample being used; this also makes decay corrections unnecessary. Any type of radiation-detecting equipment that is suitably sensitive and reliable may be used for the comparison.

These comparative measurements are most often made with counting systems because high sensitivity is usually necessary.

With gamma-emitting nuclides, the most useful instrument is the well-type scintillation counter described in section 7.6.2. For high-energy beta-emitting nuclides, the addition of a lead filter a few thousandths of an inch thick between the sample and the gamma-ray counter will increase the *bremsstrahlung* production, but care must be taken to ensure that comparative measurements are made under *identical* conditions.

8.2.4. *Low-energy beta-emitting nuclides.* For nuclides emitting beta particles of low energy, *bremsstrahlung* methods cannot be used. A thin-window or windowless counter, an ionization chamber, or a liquid scintillation counter, must then be used (sec. 7.4 or 7.6.1).

8.3. Radionuclide Identification

If radioactive materials to be used in human studies are obtained from a source that does not guarantee the identity and radiopurity of the radionuclide sample, these must be established by the user.

Ordinarily the approximate activity of a radionuclide shipment is stated, and if its assay by the user yields results in good agreement with the expected value, the identity of the nuclide is unlikely to be other than that expected. Small and usually unimportant amounts of contaminant radionuclides are to be expected in some samples. Care must be taken that these contaminants, particularly after long periods, do not compromise the nature of the sample.

The most accurate method of establishing radionuclide identity is a spectral distribution study, preferably of both beta and gamma rays. This method, however, is not easily applied to nuclides which emit only low-energy beta particles and may fail to detect such radionuclides in the presence of a gamma-emitting radionuclide.

Radionuclide identification can also be established by measurements of half-life and by absorption methods. These methods are not always conclusive and cannot be applied to all radionuclides, but nevertheless are useful. Other special methods may be necessary if it is desirable to establish the absence of certain radioactive impurities (for example, hydrogen-3). In circumstances where the identification has not been fully established, a knowledge of the target material and the production procedures may be very useful.

Methods of radio-paper-chromatography (sec. 12.6) may be useful in verifying the nature, purity, and chemical stability of labeled compounds.

8.4. Chemical Purity and Pyrogen Activity

The chemical purity, total amount of stable isotope (or carrier), and *p*H of samples that are to be administered clinically should be tested if they have not been certified by a commercial supplier. In addition, tests of sterility and pyrogen activity are required for samples that are to be administered intravenously (U.S. Pharmacopeia XV).

8.5. Measurement of Dose Rate from Small Sealed Sources

8.5.1. *General.* In many therapeutic applications of radionuclides the important quantity is the dose rate from a source or configuration of sources rather than the activity. The dose rate can be derived if the activity, the specific gamma-ray emission constant Γ (or the average beta-ray energy), and the arrangement of source material are known. It may be more convenient and more accurate, however, to measure the dose rate directly. This may be the case when gamma-emitting nuclides are used in some interstitial, intracavitary, and superficial applications, and when beta-emitting nuclides, such as strontium-yttrium-90, are used in superficial applications.

8.5.2. *Gamma-ray exposure dose rates.* If the gamma-ray sources are long-lived their activities will generally be measured and specified in millicuries and the constant Γ, the specific gamma-ray emission (app. A), can be used to calculate the exposure dose rate. Frequently gamma-ray activi-

ties are determined by a measurement of each source, using an air-wall ionization chamber as described in detail in section 3.6 and in section 8.2.22. This procedure has the advantage that any error in the value of Γ, or in the specified activity is eliminated.

In the case of shorter-lived samples (e.g., metallic gold-198 seeds, iridium-192 seeds), the activity of the individual seeds will need to be measured, unless the variations among individuals are known, in which case the activity of a group may be determined. Any gamma-ray method may be used for this purpose but the most satisfactory is a dose measurement (as above).

In circumstances where the exposure dose rate from a particular arrangement of sources is required, a detector (usually an ion chamber or scintillation counter with an anthracene crystal) should be used which is direct reading and calibrated for the radiation of interest in terms of exposure dose rate. Techniques are described in texts on radiological physics [e.g., Hine and Brownell, 1956].

8.5.3. *Beta-particle absorbed dose rates.* Standardization of beta-emitting applicators (such as strontium-yttrium-90 plaques) requires a dose-rate rather than a disintegration-rate measurement. Owing to scattering and beta-ray absorption, it is difficult to calculate the dose rate from such a source even when the activity content is known. (See Hine and Brownell, 1956, ch. 16, "Discrete Radioisotope Sources" by R. Loevinger, E. M. Japha, and G. L. Brownell.) Generally a depth-dose curve is also required; i.e., the dose rate as a function of distance in tissue from the face of the applicator.

Dose rate determinations may be accomplished, using the Bragg-Gray principle, by measurement of the ionization in a narrow air-gap situated at the face of the applicator (to determine the surface dose) or with a uniform layer of absorbing material interposed (to determine the depth dose). Both the absorber and the material from which the ionization chamber is constructed should resemble tissue in their interaction with beta-particles, and in this respect most plastics are satisfactory. The measured intensity of ionization varies considerably with the width of the gap, and chambers of the extrapolation type are often used [Failla, 1937; Bortner, 1951; Krohmer, 1951; Failla and Gross, 1952; Loevinger, 1953]. In these, the spacing of the electrodes can be varied, and the results are extrapolated to zero gap-width. Chambers of fixed width [e.g., Sinclair and Blondal, 1952] are very much simpler to construct, and more rapid in use. It may be possible to estimate the error introduced by the finite width

of the chamber, from published results on extrapolation chambers. Failla and Gross, and Loevinger find that the extrapolation is linear over only a very narrow range of electrode spacing, e.g., up to 0.02 cm with an applicator 0.7 cm in diameter. Haybittle [1955] obtains a much greater linear range by surrounding the collecting electrode with a guard ring of comparable width, and so reducing edge effects.

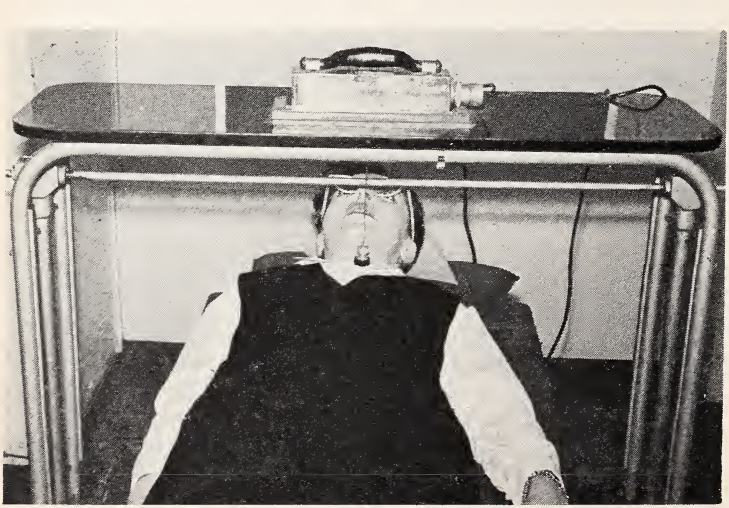
Measurements of this type are very difficult and, consequently, commercial sources should always be obtained with a calibration. For details of the methods of measurement, the references listed above should be consulted.

9. *In Vivo* Measurement—Quantitative Studies

9.1. General

The difficulties in the techniques of measuring a radioactive deposit *in vivo*, as compared with the measurement of a liquid, solid, or gas sample, are due to a variety of additional complicating factors. These factors include the location of the radioactive material in the body, the anatomical variations in size and position of the organ containing the radioactivity, and the variations in activity concentration both within the organ itself and in the surrounding tissues.

In vivo measurements are generally accomplished by means



IGURE 9.1–1. *Assembly for uptake measurements using a shielded bismuth-coated Geiger-Müller counter mounted on a hospital over-the-bed table with height adjustable by a crank.*

of a collimated detector placed at a suitable distance from the region of interest. (See fig. 9.1–1. and 9.1–2.). Usually only gamma radiation (and occasionally *bremsstrahlung*) is studied in this way, although sometimes it is possible to make *in vivo* measurements at the surface of the body with a beta counter and in tissues with a needle-type counter. *In vivo* measurements of beta radiation are usually only relative to each other and only very approximate quantitative estimations are made.

9.1.1. *Collimation and shielding.* The purpose of collimation is to exclude both general background radiation and radiation from areas of the body other than the region of interest (often called "body background"). The amount of shielding required must be carefully considered because it is desirable to keep the bulk and mass of the detecting probe

FIGURE 9.1–2. *Uptake assembly for tracer doses of 10 to 50 microcuries of iodine-131.*

Assembly for uptake measurements using a scintillation counter. To the collimating shield of the scintillation counter is added a curved lead sheet to reduce the contribution from body background. [Courtesy of S. Feitelberg.]

as small as possible in order to retain flexibility in probe location. The probe is, furthermore, frequently balanced at the end of an adjustable arm. The shielding thickness should be chosen so that the radiation reaching the detector through the shielding is only a small fraction of the radiation reaching the detector through the aperture. A maximum of 1 percent for this fraction is a desirable figure, but since the solid angle of the aperture is often a small fraction of 4π, attenuation factors for the shielding of 10^3 to 10^4 may be necessary in order to achieve this. With iodine-131, from 1 to 2 in. of lead are often used. In some circumstances, when a large aperture is used, less shielding may be possible, but in others, particularly when a very small aperture is used, more shielding may be necessary (see fig. 9.1–3.).

Materials of high atomic number and density are most suitable for gamma-ray shielding, particularly for low-energy gamma rays (for example, from iodine-131 and gold-198). Because of the difficulties of providing sufficient shielding, except in a very bulky, massive apparatus, high-energy gamma rays (for example, from cobalt-60, iron-59, potassium-42, sodium-24) present much greater problems for *in vivo* measurement.

9.1.2. *In vivo detectors.* In most human *in vivo* studies it is desirable to use the smallest practicable amount of radioactive material in order to reduce the dose to the patient to

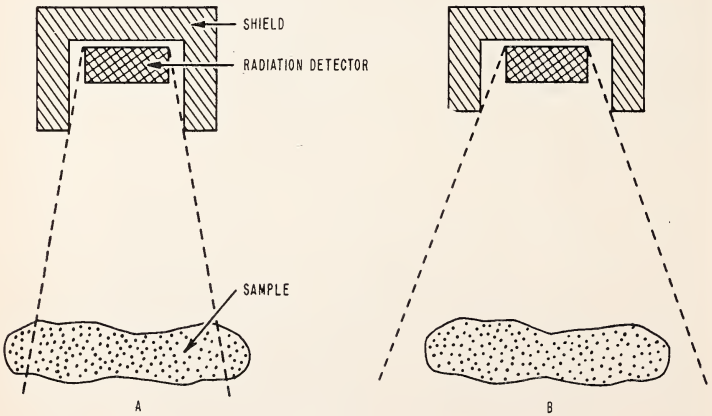


FIGURE 9.1–3. *Shielding of an uptake counter.*

This assembly is suitable for tracer doses of about 1 microcurie of iodine-131. The shield is mounted on the stand of a dental X-ray machine. (A) excessive collimation, observed counting rate will be too low. (B) suitable shielding, all of the organ contributes to the observed counting rate [Quimby, Feitelberg, and Silver, 1958; courtesy of Lea and Febiger].

a minimum, and consequently the sensitivity of the detector should be as high as possible. (The sensitivity of the *in vivo* detector, however, may not always be the determining factor in the amount of radioactivity necessary for a tracer test; other clinical, biological, or technical factors may require that relatively large amounts be administered. In such cases a simpler, smaller, or less efficient *in vivo* detector may be adequate.) The most sensitive detectors are of the scintillation type, using large sodium iodide crystals ranging from 1 to 3 in. in diameter.

The thickness of the crystal used may vary, but for low-energy gamma radiation the efficiency increases slowly with increasing crystal thickness. For gamma rays of 0.4 Mev (which is the approximate average energy of the radiations from both iodine-131 and gold-198), the percentage of the incident radiation absorbed in a sodium iodide crystal varies with crystal thickness as follows:

½-in.-thick crystal	40% absorbed
1-in.-thick crystal	63% absorbed
2-in.-thick crystal	87% absorbed
3-in.-thick crystal	95% absorbed.

However, the background increases proportionally with the thickness (assuming the same shielding), and consequently the true-count-to-background ratio actually decreases. Therefore, with iodine-131, for example, the use of sodium iodide crystals thicker than 1 to 2 in. is of little additional value.

For uptake studies a scaler is frequently used with the detector and probe, and perhaps also a pulse-height analyzer, but when variation of uptake or distribution with time is important it is more convenient to use a ratemeter and recorder (sec. 11).

9.2. Measurement of Iodine-131 Uptake in the Thyroid Gland

The measurement of iodine-131 uptake in the thyroid gland is currently the most important *in vivo* medical procedure involving quantitative estimation of radioactivity. Many other tests may be used either in addition to, or instead of, uptake measurements to determine thyroid function, but a discussion of these is outside the scope of this handbook. The reader is referred to texts on the subject, e.g., Quimby, Feitelberg, and Silver [1958], Beierwaltes, Johnson, and Solair [1957], and a recent group of articles, Goldberg and Fitzsimons [1958], Goolden [1958],

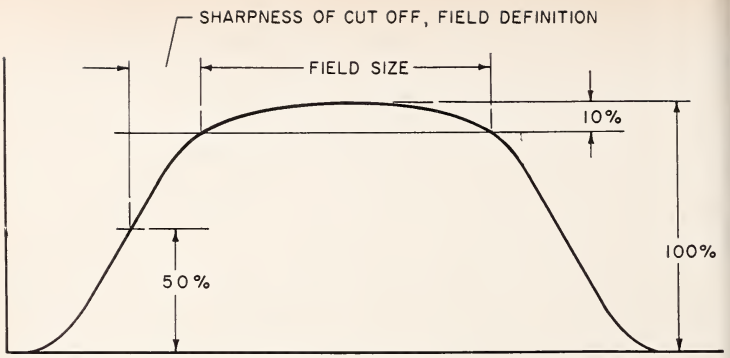


FIGURE 9.2–1. *Transmission of collimator as determined by moving a point source of radiation on a plane at the working distance.*

Howard, McAlister, and McEvedy [1958]. The measurement of radioiodine uptake in the thyroid may be subject to many errors unless account is taken of the important factors involved [Brucer, 1955]. These factors are discussed in detail by Feitelberg [Quimby, Feitelberg, and Silver, 1958, ch. XVI, "Quantitative Measurements *in Vivo*"] and are summarized here to exemplify the principles of measurements of this type.

9.2.1 *Size of gland.* The radiation detector must be adequately shielded from body background radiation, but it must have a field of view to admit radiation from the largest gland. Excessive collimation gives false low readings with large glands. The field size required is 6 to 8 in. in diameter. The size of the field may be determined geometrically or it can be checked with a point source of radiation which is moved on a plane at the working distance.

Since the drop in sensitivity towards the edges of the field is not sharp, due to the umbra and penumbra of the collimator, for practical purposes the field size is defined as that area where sensitivity varies within a given range, for instance, 10 percent. Field definition, i.e., the sharpness of the cut off in sensitivity beyond this area has to be considered also; this may be defined as the distance of half-sensitivity area from the field edge and should not exceed 10 to 25 percent of the field diameter (see fig. 9.2–1.).

9.2.2. *Body background.* When radiation from the body penetrates the shield, false high readings result. This contribution to the background from the radioactivity in the body can be determined by shielding the field of view of the counter with a lead sheet (1- to 2-in. thick) of a size corre-

sponding to this field. If the lead shield around the detector is adequate, this contribution should be very small. The effect is most important when measurements are made within a few hours of administration of the radioactive material, particularly when the percentage uptake in the gland is low, and also in the majority of cases of high thyroid radioiodine turnover when, after 48 to 72 hours, the total body radioactivity is high.

In addition to radiation from the body outside the thyroid gland, the readings are increased also by radioactive material in the circulating blood. A correction for this can be applied by measuring the activity over the thigh with the same detector and subtracting this value from the thyroid measurement; this correction is, however, of moderate value, because of the higher vascularization of the thyroid gland as compared with muscles. Many investigators feel that it is a better approach to measure the thyroid uptake, whenever possible, about 24 hours after administration of the tracer dose, when iodine levels in circulating blood drop to a negligible level for external counting.

9.2.3. *Depth of gland below skin of the neck.* The detector can be positioned with precision only with reference to the skin. Variations of the gland location will result in variations of the effective distance of the gland from the detector and in variations in absorption by the overlying tissues.

Variation of distance: The effect of this variation can be reduced by increasing the distance of the counter from the neck. Too great distance is impractical, since the counting rate in the detector falls and the aiming of the collimator becomes more critical. A useful compromise appears to be a distance between 20 and 30 cm. Means should be provided for ensuring that the distance chosen is reproducible.

Variations due to differences in absorption: There is no way to reduce these variations by counter construction; the effect can be reduced, however, by the method described in the next paragraph.

9.2.4. *Scattered radiation.* Scattered radiation from the gland itself and from the surrounding tissues increases the number of quanta reaching the detector: (1) as compared to the number of quanta reaching the detector when the same activity is suspended in air; and (2) when the gland is deeper in the neck (back and forward scatter) as compared to the gland at the surface (backscatter only).

Scattered radiation from the body makes it necessary to calibrate a counter in terms of a reference sample of iodine-131 in a suitable phantom. Such a phantom should be not

smaller than a cylinder 6 in. in diameter and in height, made of water, plastic or hardwood. The reference sample should be at a depth below surface approximating the average depth of the gland in the neck (½ to 1½ cm) and should be of comparable volume with the gland to be measured (25 to 50 ml). This reference sample is usually an aliquot from the same stock solution, or a capsule from the same batch, as the administered sample. The contribution of backscattered radiation to the counting rate can be reduced or eliminated by use of lead filters, $\frac{1}{32}$- to $\frac{1}{16}$-in. thick, in front of the collimator or by use of a suitably high discriminator setting with a scintillation counter or by use of a scintillation spectrometer. Any of these methods reduces the sensitivity and makes longer counting necessary.

The increase in the proportion of scattered radiation counted with greater depth of the gland in the neck tends to compensate for the decrease of counting rate due to greater distance from the detector and due to greater absorption by the overlying tissues. When the radiation detector maintains its sensitivity to scattered radiation, the dependence of the observation on the uncertain depth of the gland is reduced.

If the detector is sensitive to scattered radiation, it is particularly important that the phantom (and standard) used for comparison duplicate closely the geometry of the thyroid to be measured. If the gland (or neck) is of unusual size and it is impractical to compare it with a normal standard, a more precise measurement *may* be made by excluding scattered radiation as above.

9.2.5. *Recommended procedure.* In view of the complexity of factors entering into an accurate determination of thyroid uptake, the variety of equipment in use, and the variety of clinical circumstances that may be encountered, it is difficult to recommend a procedure that will offer the greatest accuracy in all circumstances. The importance of evaluating the characteristics of each thyroid-uptake apparatus under all possible conditions of use and of correcting for possible deficiencies such as inadequate shielding, cannot be overemphasized.

It is felt, however, that the following procedure may be the most generally useful for the scintillation equipment most commonly employed today, and this procedure is therefore recommended:

1. The radiation detector is positioned 20 to 30 cm from the patient's neck in a reproducible position.
2. A collimated shield is used with a field of view of 6 inches in diameter at a working distance of 20 to 30 cm.

3. When uptake measurements are made with high body background (a few hours after a tracer dose or in some cases at 48–72 hours), this background is evaluated by placing a lead shield of 1- to 2-inch thickness covering the field of view of the counter.
4. The calibration of the counting equipment under working conditions is made by using a suitable phantom with a source of comparable size at the same effective distance.
5. Counter sensitivity to low-energy, scattered radiation is maintained (except as noted in section 9.2.4.).

9.2.6. *Multiple-detector systems.* A basically different approach is to use several counters in a ring array instead of a single counter. The patient is positioned with the neck approximately in the center of this array. The counters are connected through a mixing circuit to a scaler, which registers the sum of counts in all counters. This arrangement reduces the dependence of the counting rate on gland depth and on patient movements (no immobilization of the patient is needed), but the reported results do not seem to justify the greater expense where scintillation counters are used. [Brownell and Stanbury, 1953.]

9.3. Quantitative Estimations in Organs Other Than the Thyroid

The estimation of radioactive content in organs other than the thyroid has so far been of lesser medical importance but is nevertheless sometimes of interest. It may be desired, for example, to determine the amount of radioactive material retained in the intact liver or spleen, or the amount of radioactive material accumulated in a distant metastasis of the thyroid gland. The basic considerations discussed in section 9.2 still apply. The technique of comparison with the detector in the same relation to a phantom duplicating the *in vivo* situation as closely as possible should be used whenever practicable. The larger the region of radioactive concentration under consideration, the more important it is that the reference sample be of comparable size. For example, in order to make an estimate of the amount of iodine-131-labeled compound retained in the liver, a duplicate of the shape and size of the liver (determined by palpation, or even better, by means of distribution studies as in section 10, since these will give the size of the region actually concentrating radioactive material) should be made in wax or other suitable material and filled with a known amount of iodine-131 and then immersed at the appropriate depth

in a water phantom of suitable size. A comparative measurement over patient and phantom with the collimated detector will then give a reasonable estimate of the amount of activity in the unknown region.

9.3.1. *Differences in technique from thyroid uptake study.* The following points of difference from techniques used for thyroid uptakes should be noted:

1. The field of view of the detector will generally need to be larger.
2. The size and shape of the reference sample must be similar to that of the region studied. (Distribution studies as in sec. 10 may be very helpful.)
3. The background from other parts of the body is likely to be relatively more important because the concentration in the region under study is usually much lower than in the thyroid. Therefore better shielding or more detailed correction for body background may be necessary.
4. The distribution of the radioactive material in the region may vary greatly (see sec. 10 for methods). In an organ of large size, this may reduce the accuracy of the phantom comparison.

9.4. Estimation of Whole-Body Radioactivity in Humans and Animals

Some gamma-ray measurements can be conducted by the inclusion of the whole animal or human body within the detecting device. Most of the equipment is designed to meet individual problems. In certain instances, the technique is one of considerable importance and usefulness.

9.4.1 *Detectors.* The detector may be of any of the basic counting or ionization-chamber systems. Each has some useful features. Since the whole-body-counting technique is especially useful for low-level counting estimations, the most important factors are high sensitivity, stability, uniform sensitivity of the measuring system, and adequacy of shielding for background reduction. If identification of radioactive material is required, resolution must also be considered.

9.4.11. *Geiger-Müller detectors.* Geiger-Müller counting systems are useful for small animals. Counters arranged in a circle or single counters with multiple anodes have been used for whole-body counting of rats and mice.

9.4.12. *Ionization detectors.* Ionization-chamber systems involving pressure chambers for total body counting of humans offer a system of high stability but limited

sensitivity (2×10^{-9} g of radium-226) [Sievert, 1951; Burch and Spiers, 1953; Rundo, 1955].

9.4.13. *Scintillation detectors.* Scintillation systems of two types are in use:

9.4.13.1. *Total enclosure counters using a liquid luminescent medium with a large number of phototubes.* Systems for rat counting, dog counting [Van Dilla, Schuch, and Anderson, 1954], and human counting [Reines, Schuch, Cowan, Harrison, Anderson, and Hayes, 1953] offer very high sensitivity (sufficient to detect the potassium-40 radioactivity of the human body to about 5-percent accuracy in a single count of 100 sec), reasonable stability, and easily reproducible geometry. They have poor resolution, however, and are therefore of limited value if the nature of the radioactivity is to be identified (see figs. 9.4–1. and 9.4–2.).

9.4.13.2. *Discrete detector in a fixed position.* Single crystals or groups of crystals of thallium-activated sodium iodide have been used for this purpose, ranging in size up to

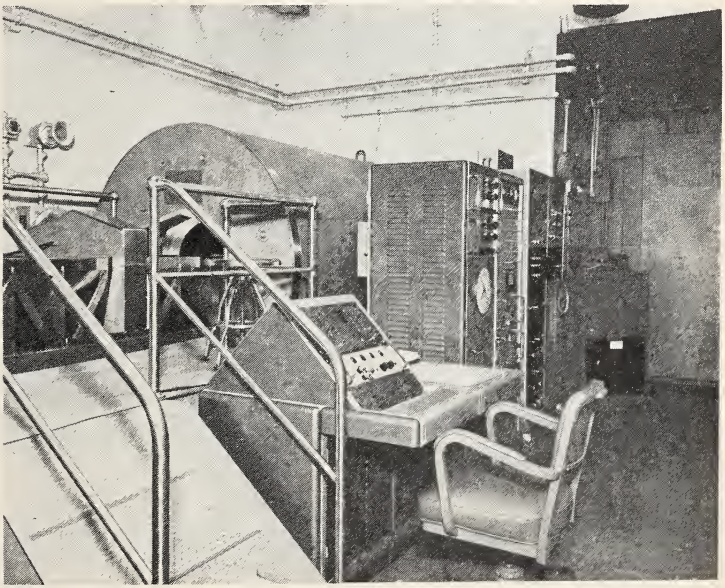


FIGURE 9.4–1. *Overall view of the whole-body-counting facility at the Walter Reed Army Institute of Research.*

On the left is the liquid scintillation counter, on the right, background, is the steel room containing the 8×4-inch sodium iodide crystal spectrometer. [Courtesy Walter Reed Army Medical Center, Washington, D.C. (U.S. Army Photograph).]

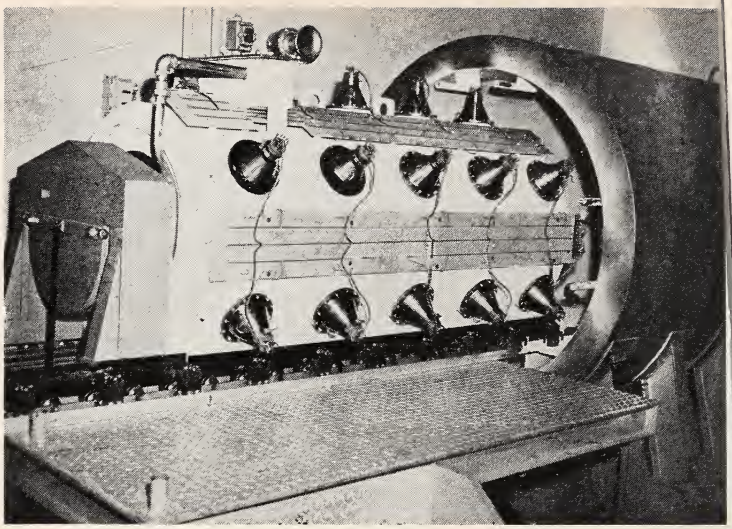


FIGURE 9.4–2. *Whole-body liquid scintillation counter at the Walter Reed Army Institute of Research with the detector tank partially withdrawn, showing some of the 30 5-inch photo-electron multiplier tubes.*

The liquid scintillator consists of terphenyl and POPOP in toluene. [Courtesy Walter Reed Army Medical Center, Washington, D.C. (U.S. Army Photograph).]

8 in. in diameter by 4 in. thick [Marinelli, Miller, Gustafson, and Roland, 1955] and larger. The establishment of a reproducible geometry is more difficult than in the totally enclosed detector method. It is, however, particularly useful for human counting, since it has both very high sensitivity and high resolution enabling the identification of the radionuclides (see fig. 9.4–3.).

9.4.2. *Detector shielding.* The most sensitive techniques require extensive detector shielding and, for human counting particularly, represent very costly installations. For techniques involving radionuclide identification, multichannel spectrometers are necessary.

For determinations of rate of excretion, by total-body measurements, the distribution of the material must remain substantially constant, unless the detector is insensitive to the changing position of the radioactivity within the body.

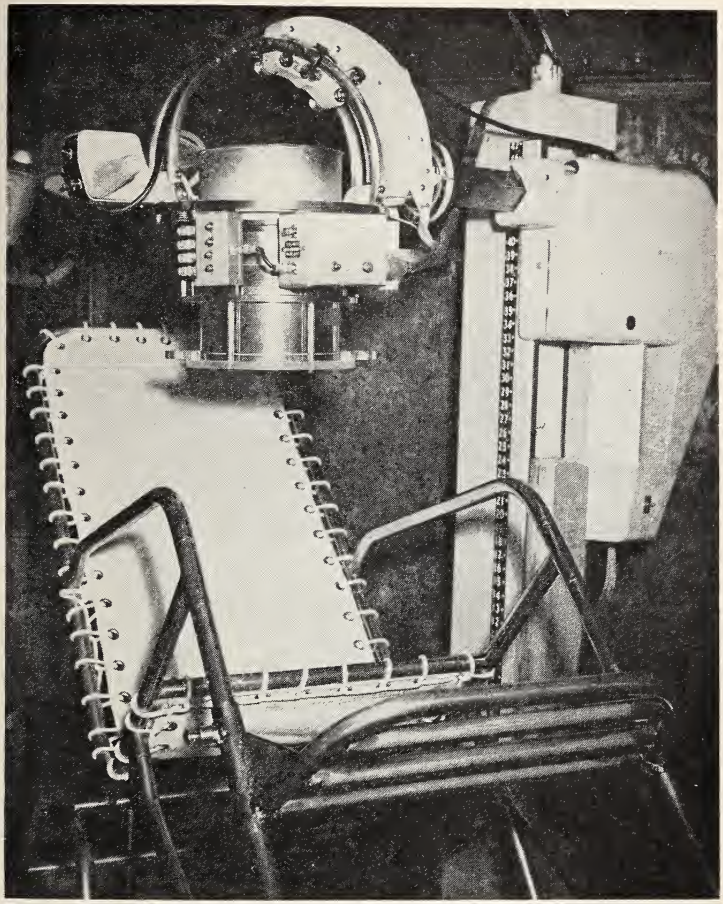


FIGURE 9.4–3. *The 8 × 4-inch sodium-iodide crystal in the Walter Reed Army Institute of Research steel room.*

This room consists of armor-steel plates built to give a total wall thickness, for shielding, of seven inches of steel. The crystal is shown in the human whole-body counting position. [Courtesy Walter Reed Army Medical Center, Washington, D.C. (U.S. Army Photograph).]

10. *In Vivo* Counting Methods—Distribution Studies

10.1. General

Knowledge of the distribution of a radionuclide within the body of a patient is frequently of clinical value. The information required may simply be the presence or absence of a concentration of the nuclide in question, as in the case of metastatic thyroid carcinoma, or it may be precise delineation of the size and shape of the radionuclide deposition, as in the case of studies of the thyroid gland.

This information is most often obtained by external counting of the patient in the case of gamma emitters. A survey, or scan, is made by systematically moving a radiation detecting instrument over the region of interest, which may be the patient's whole body, and recording the count rates obtained.

Scanning measurements are generally not quantitative because of the difficulty of determining the depth and volume in which the activity is concentrated. Relative measurements, however, are often extremely valuable. Estimates of the amount of radioactivity involved can sometimes be made if comparable calibrated phantoms are studied.

Scanning methodology has been considered generally from a theoretical standpoint [Brownell, 1958] and with respect to problems of instrumentation [Brucer, 1958].

10.1.1. *Applications.* Many applications of scanning techniques have been reported and, while a detailed discussion of applications is outside the scope of this handbook, the following brief summary cites some representative references in the field which may be of value to the reader.

Most studies have been made of the thyroid with iodine-131 as the tracer isotope [Bauer, Goodwin, Libby, and Cassen, 1952]. A scanning study allows visualization of the functioning thyroid tissue and may differentiate between normally and abnormally functioning areas. Similarly, sublingual and mediastinal thyroids may be identified [Feitelberg, Kaunitz, Wasserman, and Yohalem, 1948; Miller and Scofield, 1955; Kuhl, Chamberlain, Hale, and Gorson, 1956]. In metastatic thyroid carcinoma, functioning metastases may be located and their metabolic activity may be studied [Frantz, Ball, Keston, and Palmer, 1944; Catz and Starr, 1956; Kuhl, Chamberlain, Hale, and Gorson, 1956]. By injecting compounds that are concentrated in the liver (colloidal gold-198; iodine-131-labeled tetraiodophenolphthalein or rose bengal), it has been possible to detect metastatic areas in the liver [Yuhl and Stirrett,

1953; Yuhl, Stirrett, and Cassen, 1953; Friedell, MacIntyre, and Rejali, 1957]. Studies of the apparent uniformity of distribution of intracavitary instillations of colloidal gold-198 have been reported [Kuhl, Chamberlain, Hale, and Gorson, 1956]. Because iodine-131-labeled diiodofluorescein concentrates in the normal gall bladder, gall bladder function can be demonstrated by external scanning [Yuhl, Stirrett, Hill, and Beal, 1953]. Iodine-131-labeled human-serum albumin has been used to study, by scanning methods, localization in brain tumors [Allen and Risser, 1955; Shy, Bradley, and Matthews, 1958], the patency of the subarachnoid space [Bauer and Yuhl]; [quoted by Yuhl, Stirrett, and Cassen, 1953], and blood pools [Rejali, MacIntyre, and Friedell, 1958].

10.2. Manual Scanning

10.2.1. *Equipment for detection.* Hand-held or stand-mounted Geiger-Müller counters or scintillation counters are systematically moved over the areas of interest. Often the information sought is simply the presence or absence of detectable amounts of radioactivity. The design of equipment is not considered critical [Feitelberg, 1955], but the optimum design of hand-held counters for scanning has been considered [Corbett and Honour, 1951].

Frequently, useful information can be obtained by comparing the count rate obtained over an area of interest to the count rate obtained over a symmetrically located normal area. If care is taken in repositioning the counter on successive occasions, the metabolic activity of the area of interest can be estimated [Frantz, Ball, Keston, and Palmer, 1944].

10.2.2. *Recording counting information.* The count rate variation, as the counter is moved over the patient, may be monitored by aural signals, visually with count-rate meters, or by recording accumulated counts over a short period of time. Usually a grid pattern, which may be from ¼ to 1 in., is used for establishing counting positions. Counts are recorded for each grid position. A system of "control point values" related to anatomical landmarks has been advocated [Stirrett, Yuhl, and Libby, 1953]. More often isocount-rate curves are drawn corresponding to the counts recorded on the grid positions [Pochin, 1950; Cassen, Curtis, Reed, and Libby, 1951; Allen, Libby, and Cassen, 1951; Blomfield, 1951]. Alternatively, a counter equipped with a count-rate meter may be moved to hunt for preselected count-rate levels and the grid used to record the positions of the isocount contours [Chamberlain, 1953].

10.3. Automatic Scanning

In automatic scanning apparatus, the radiation detector is moved mechanically in a preset pattern over the patient's body. The basic equipment needed is a radiation detector with appropriate shielding and collimation, a mechanical system for moving the detector, counting equipment, and equipment for recording the information obtained. A block diagram of such an arrangement is shown in figure 10.3–1.

10.3.1. *Radiation detectors.* Scintillation counters with thallium-activated sodium iodide crystals are generally used in scanning equipment. Because the mass of the lead shielding must be held within practical limits, crystal diameters are usually about 1 or 2 in. The optimum crystal thickness depends on the gamma-ray energy of the nuclide being used; for iodine-131 a crystal thickness of 1 in. is often used, though ½ in. is probably sufficient for many applications [Kuhl, Chamberlain, Hale, and Gorson, 1956; Jansson, Larsson, and Raynholt, 1957; Friedell, MacIntyre, and Rejali, 1957]. Considerations of crystal thickness are discussed in section 9.1.2.

Side shielding is more critical for scanners than for uptake counters or sample counters because frequently the amount

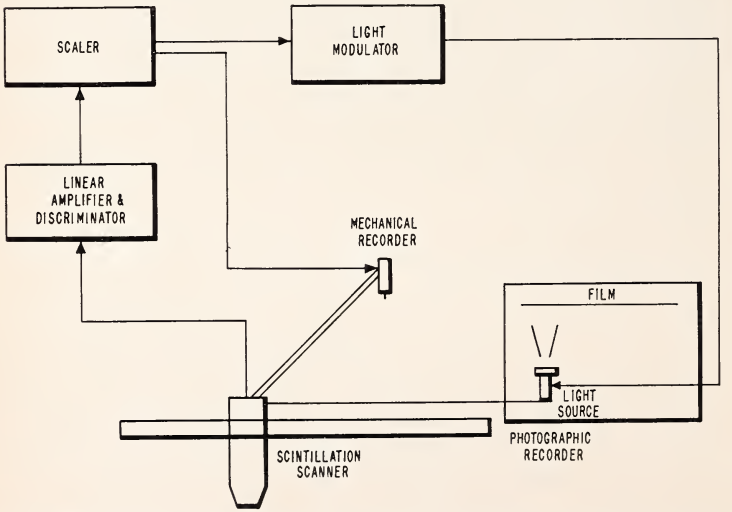


FIGURE 10.3–1. *Block diagram of scanner with two types of recording system.*

Motors drive the radiation detector and connected recording apparatus over the patient in a two-dimensional rectangular pattern. [Kuhl, Chamberlain, Hale, and Gorson, 1956; courtesy of Radiology.]

of radioactivity "seen" by the counter is much less than is present elsewhere [Mayneord and Newberry, 1952]. The required thickness for shielding depends on the energy of the gamma rays being measured, and even for iodine-131 a thickness of more than 1 in. of lead may be necessary (the initial half-value layer in lead is approximately 0.3 cm).

A wide variety of suitable crystal sizes, phototubes, and preamplifiers is commercially available.

10.3.2. *Collimators.* Collimator design for scanning equipment must strike a suitable compromise between sensitivity and resolution. Sensitivity (expressed as net counts per unit time per unit of radioactivity) is important when attempts to detect marginal concentrations of activity are made. The theoretical resolution is expressed as the linear width between the half maximum points of the curve obtained by moving a point or line source under the collimator and indicating, thereby, the minimum separation necessary to distinguish two sources. This resolution is related to the ability of the scanning equipment to determine detail in the area of concentration.

The most commonly used collimator for two-dimensional motion scintillation scanning is the straight-bore type, the apertures of which vary from ½ to 1 in. in diameter. The collimator length is generally between 5 and 12 cm [Kuhl, Chamberlain, Hale, and Gorson, 1956; Jansson, Larsson, and Raynholt, 1957; Friedell, MacIntyre, and Rejali, 1957]. Some idea of the effects of the variables of aperture diameter and length can be obtained from table 10.3–1 [Kusner, 1956].

Various special collimator designs have been investigated; for example, single channel conical, spiral, multiple parallel channel, and focused multiple channel [Newell, Saunders, and Miller, 1952; Miller and Scofield, 1955; Shy, Bradley, and Matthews, 1958]. Typical data regarding some of these designs are contained in table 10.3–2.

TABLE 10.3–1. *Resolution of straight-bore collimators*

Narrow-angle, single-channel, straight-bore collimators
capillary line source 4 cm from collimator tip

Crystal size (in.)		Collimator diameter (in.)	Collimator length (cm)	Resolution (½ width) (cm)
Diameter	Height			
¼	¼	¼	3.0	2.0
½	½	½	6.2	2.7
1	1	½	12.5	2.0
1	1	1	10.0	3.8

TABLE 10.3–2. *Resolution and sensitivity of collimators*

Collimator type	Source collimator distance (cm)	Sensitivity (c/sec/μc)	Resolution (½ width) (mm)
Wide angle, straight bore 3″ diam × 5-cm long	3	100	85.0
	7	51	116.0
	10	28	132.0
	13	24	146.0
Cone bore, 5-cm top, 1.5-cm bottom aperture; 5-cm long	3	32	29.5
	7	23	32.5
	10	11	40.0
	13	6	55.0
Focused multiple channel, 61 channels, 5-cm long	3	9	22.5
	7	13	13.7
	10	14	11.2
	18	10	13.0

The design of collimators for one-dimensional motion (profile) scanning is somewhat different. It is desirable to have good resolution along one axis and complete acceptance along the other axis. A collimator has been designed, for example, that has a long axis resolution of 2 cm at a 13-cm source-crystal distance and, with the addition of a wedge filter, a uniform response for about 40 cm in the short-axis direction [Concannon and Bulluis, 1957].

10.3.3. *Mechanism for moving radiation detector.*

10.3.31. *One-dimensional motion.* In this type of scanning (also called profile scanning) the radiation detector is driven by an electric motor in only one direction over the patient. A profile may be taken over either the long axis or short axis of the patient [Feitelberg, 1948; Pochin, Myant, Hilton, Honour, and Corbett, 1952; Cunningham, Hilton, and Pochin, 1955; Miller and Scofield, 1955; Corbett, Cunningham, Halnan, and Pochin, 1956; Jansson, Larsson, and Raynholt, 1957]. The method is particularly useful [Cunningham, Hilton, and Pochin, 1955] because it allows quantitative study of the metabolic turnover of the radionuclide in the volumes of interest and allows routine whole-body surveys to be made in a reasonable period of time.

Scan speeds vary from 2 to 30 cm per min. The most commonly used speeds are between 4 and 10 cm per min.

10.3.32. *Two-dimensional motion: Rectangular.* The most frequently used pattern for moving the radiation detector over the patient is a two-dimensional rectangular pattern. The counter is moved across the short axis of the patient at a pre-set speed. At the end of each scan line, the counter is advanced along the long axis of the patient for a pre-set distance [Cassen, Curtis, Reed, and Libby, 1951;

Mayneord, Evans, and Newberry, 1955; Sopp, Geyer, and Lehman, 1954; Kuhl, Chamberlain, Hale, and Gorson, 1956; Friedell, MacIntyre, and Rejali, 1957; Jansson, Larsson, and Raynholt, 1957].

Scan speeds vary from 14 to 120 cm per min. The most commonly used speeds are from 30 to 60 cm per min. Line spacing varies between 0.3 and 27 mm. For scanning small areas (thyroid), 0.5- to 3-mm spacings are used. Most scanners are designed to cover as large an area as possible with one adjustment of the mechanism; 14×17 in. is usually thought to be sufficiently large.

The optimum choice of scan speed and line spacing involves a practical compromise between the quality of the final scan picture and the time required to perform the scan, and will depend on the sensitivity of the radiation detector, the amount of the radioactivity in the volume scanned, and the size of the area scanned. In general, when small areas are scanned (thyroid, for example) it is practical to use slower scan speeds and smaller line spacing than with large areas.

Localization of the radionuclide-concentrating volume can be determined with greater accuracy if the projection of the volume can be scanned in two planes at right angles. Scanning apparatus can be designed [Kuhl, Chamberlain, Hale, and Gorson, 1956] to rotate about an axis for this purpose.

In order to decrease the time required to scan a large portion of the body, systems of multiple counters have been used. A strip 7-in. wide can be scanned during a single cross-travel sweep by using 10 scintillation detectors [Anger, 1953].

10.3.33. *Two-dimensional motion: Radial.* A scheme of radial motion by which a single detector scans the patient from a distance while being moved in a radial pattern over the area of interest has been developed [Mayneord and Newberry, 1952; Mayneord, 1953].

10.3.34. *Two-dimensional motion: Two oppositely mounted detectors.* For the scanning of regions such as the head, systems using two oppositely mounted detectors moving in unison have been found particularly useful. The motion used may be rectangular [Brownell and Sweet, 1953; Sweet and Brownell, 1955] or radial [Reid and Johns, 1958]. These systems may be used to count coincidences (which is particularly useful in the case of the annihilation radiation from positron emitters as used by Sweet and Brownell), to count in each detector independently, or to subtract the count rate due to one detector from that of the other, thus providing additional information about the depth of a radioactive concentration.

10.3.35. *No motion: Multiple detectors.* An adaptation of the simple pinhole camera has been used to photograph the distribution of radioactivity in patients [Anger, 1952]. A thallium-activated sodium iodide flat plate crystal is used as an intensifying screen. The camera has a ⅛-in. aperture for the pinhole. A more complicated system uses a pinhole camera with an electronic light intensifying system added [Anger, 1958]. An array of seven phototubes views a ½-in.-thick flat plate thallium-activated sodium iodide crystal which sees the area containing radioactivity through a ¼-in. diameter pinhole aperture. The proportional output from the various tubes due to a single scintillation in the crystal is used to establish the x and y coordinates of the spot on a cathode-ray oscilloscope. The face of the oscilloscope is photographed to produce images made up of many such single spots.

10.3.4. *Counting equipment.* The requirements for electronic counting equipment have already been discussed (sec. 7.3.). In scanning systems, binary scalers are frequently used so that the rate of the derived pulses used to drive the recording system can be varied in fine steps to suit the requirements of the apparatus for producing an adequate image.

Pulse discrimination is used to minimize the number of scattered gamma rays that are recorded, thereby increasing the resolution of the system. Pulse-height selection systems using pulse-height analyzers have been used to further discriminate against scattered photons from the patient [Francis, Bell, and Harris, 1955]. The addition of this equipment to conventional equipment will increase the resolution of the system at some expense of sensitivity. For iodine-131, counting only the pulses corresponding to the 364-kev photopeak may increase the ratio of significant counts to background by about 1.5 [Allen and Risser, 1955]. Lead filters on the scintillation detector (about 0.5 g/cm^2) have also been used to discriminate against scattered radiation [Miller and Scofield, 1955; Friedell, MacIntyre, and Rejali, 1957].

Discriminator, high voltage, and scale-factor settings must be established for each patient to obtain the optimum derived pulse rate for image formation, because the amount of radioactivity in the area scanned and the location of the concentrating volume vary over a wide range.

10.3.5. *Apparatus for recording counting information.*

10.3.51. *One-dimensional motion.* One-dimensional, or profile, scanners ordinarily use ratemeters to measure the variation of count rate as the counter is moved over the patient. The most convenient way to record the informa-

tion is with a strip chart recorder [Miller and Scofield, 1955; Corbett, Cunningham, Halnan, and Pochin, 1956].

10.3.52. *Two-dimensional motion.* The recording system of most scanners consists of a marking device on an arm firmly attached to the radiation detector. As the radiation detector is moved over the body of the patient, the marking apparatus moves in exact correspondence and produces marks that are related to the rate at which a preset number of counts is accumulated by the counter. Many different types of marking apparatus have been reported:

(a) A pen marker of the type used on strip chart recorders can make a ⅛-in. signal line [Cassen, Curtis, Reed, and Libby, 1951]. Recorders having solenoid-operated punches which mark by striking the paper on which the image is recorded against carbon paper have the advantage that multiple copies of the scan can be made (fig. 10.3–2). The tip of the punch may have the form of either a dot or a short (1/16- to ⅛-in.) line. Punches can be obtained with re-

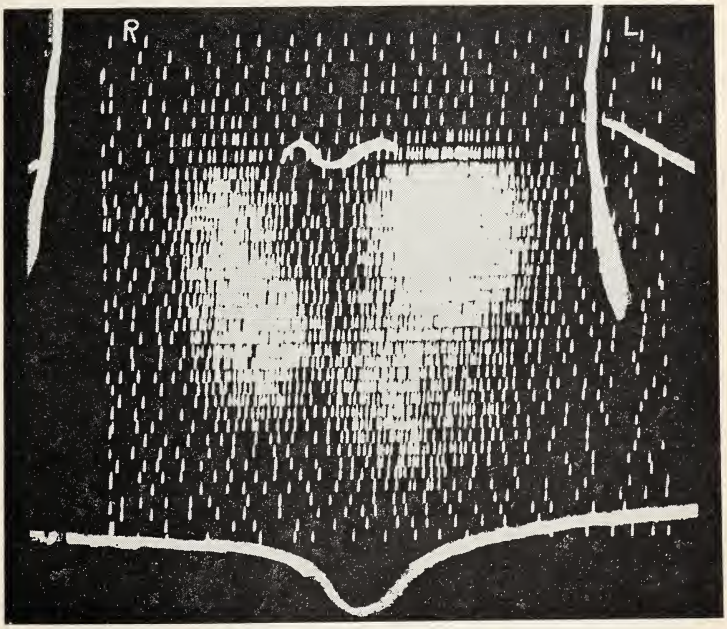


FIGURE 10.3–2. *Scan of thyroid gland* in vivo.

Recording apparatus is a solenoid-operated punch used with carbon paper. The right lobe is of normal size and configuration. The left lobe demonstrates two nodules that were palpable. One nodule shows an increased and the other a decreased concentration of iodine-131. Upon excision of the left lobe, both nodules were found histologically to be benign thyroid adenoma. [Courtesy of J. P. Storaasli.]

solving times as short as 0.3 sec [Jansson, Larsson, and Raynholt, 1957].

(b) Electrically sensitive paper has the advantage of fast resolving time [Jacobs, Orvis, and Borrman, 1954; Friedell, MacIntyre, and Rejali, 1957]. This paper is activated by passing an electrical current derived from the counter through a needle point above the recording paper to a grounded base plate.

(c) The marking apparatus may be a light that is made to flash by the counting system and record on film. This system has the advantage of no inertia, fast resolving time, and, since the light flashes overlap on the short axis, an increase in the density range is obtained. One simple system uses a strobatron light and records on inexpensive enlarging paper [Horowitz and Lofstrom, 1955]. This system, however, does not attempt to construct a solid image. The image can be better visualized if the light mark just fills the space between successive scan lines with no long axis spacing or overlap. A rectangular-shaped light spot—2 x 10 mm, with 2-mm line spacing for small area scans, and 12 x 12 mm, with 12-mm line spacing for large area scans—has been found to be suitable [Kuhl, Chamberlain, Hale, and Gorson, 1956].

Recording on emulsion on a transparent film base has the advantage that accurate anatomical localization of the area of radioactivity that has been scanned can be made. In one system, an auxiliary radiographic machine is used to produce a roentgen image on the same film that was used for recording the scan [Collins, 1956]. Another system, that does not require special equipment, uses a set of lead markers fixed on the patient. The positions of the markers are established on the scan film. A conventional roentgenogram of the patient in the scanning position shows the markers and allows accurate superimposition of the scan film and roentgenogram [Kuhl, Chamberlain, Hale, and Gorson, 1956; Rejali, MacIntyre, and Friedell, 1958].

Photographic recording of an image produced on the face of a cathode-ray tube, either directly or through a memory storage tube, has also been used [Mayneord, Turner, Newberry, and Hodt, 1951, 1955; MacIntyre and Houser, 1957; Anger, 1958].

10.3.53. *Special recording devices.* Special devices to modify the recorded image have been developed. Such devices ordinarily distort the image for some special purpose so that care must be taken in the interpretation of the image so produced.

(a) One such device speeds up the cross-scan drive motor over areas of low activity by a factor of about 3. The effect is to diminish the recorded background pulses and form a sharper image of the area of activity. This system is useful in the study of nonmalignant thyroids [Curtis and Cassen, 1952].

(b) By electronically modifying the signal obtained from the counter, it is possible to produce a light signal for photographic recording whose intensity increases by a controlled amount as the count rate increases. This system effectively reduces background while greatly enhancing the contrast of the recorded image [Kuhl, Chamberlain, Hale, and Gorson, 1956; Bender, 1957].

(c) Sometimes it is desirable to modify electronically the recording system so that a small decrease in count rate will be recorded dramatically [MacIntyre and Houser, 1957]; for example, in the study of the liver with suspected metastatic carcinoma.

(d) Recording of coincidence counts from a dual detector system (sec. 10.3.34) has been used to measure the annihilation radiation from positron-emitting nuclides [Sweet and Brownell, 1955].

The recording arm may be fixed to a pantograph so that the size of the image of a large area scan (for example, the whole body) is reduced to convenient size [Jansson, Larsson, and Raynholt, 1957]. This system makes anatomical localization more difficult but effectively increases contrast by decreasing the visual angle for the interpreter.

10.4. Interpretation of Scans

Care must be taken in the interpretation of a scanning study. Uptakes of activity in local volumes sometimes appear misleadingly dramatic. More often the possibility exists that significant variations in activity concentration within the patient cannot be detected because of the finite sensitivity and resolution of the counting equipment and the effect of background radiation from radioactivity in other parts of the patient's body. Moreover, the volume scanned will ordinarily be of uneven thickness, have uneven distributions of radioactivity within it, have irregular and unsharp contours, and be surrounded by tissue containing appreciable concentrations of radioactivity. The resolution of the radiation detector, which is ordinarily based on measurements made with point or capillary line sources, with minimal scattering, with no surrounding radioactive material, and without regard for the characteristics of the recording system, is not a reliable index of the behavior of the detector

under clinical conditions. The apparent size and shape of the recorded image will depend upon the amount and distribution of the radioactivity within and surrounding the volume of interest, the characteristics of the radiation detector, the scanning speed and scan-line spacing, and the characteristics of the recording system. Experimental studies of phantoms [Walton and Sinclair, 1952; Nicholson, Wilson, and Newton, 1954] indicate the extent to which these factors are important and give illustrations of the effects to be expected.

11. *In Vivo* Counting Methods—Time Studies

11.1. General

Time studies are concerned with dynamic as opposed to static measurements. Instead of quantitative determination of the *total* accumulation of radioactive material, as in uptake studies or of point-by-point distribution, as in scans, the purpose of these studies is to discover changes in *relative* concentrations in a particular region with change in time, or to discover *rate* of movement of the radionuclide within a body.

The administration of a tracer amount of radionuclide into a complex system in dynamic equilibrium corresponds to the impression of a transient component upon such a system. The events which take place subsequently in the metabolic pools can be represented mathematically but the mathematical analysis required is complex and the presentation of these mathematical methods is beyond the scope of this manual. As a first introduction, the books written by Jaeger [1956] and Churchill [1944] are suggested. In some cases, electrical analog methods can be used to simplify the analysis.

The experimental observations are used to elucidate some of the constants necessary for the solution of the mathematical equations or for the setting up of the electrical analogs. In some cases, the experimental information required is obtained by direct *in vivo* measurement with time, as described in this section, but more often the information is obtained by sampling the system at intervals. Methods of sample assay discussed in section 12 will then be used.

For details of the application of mathematical methods to dynamic tracer studies, the reader is referred to articles and texts such as Kamen [1957], Comar [1955], Veall and Vetter [1958], Solomon [1953], Huff and Judd [1956], Robertson [1957], Berman and Schoenfeld [1956], Sharney, Wasserman, Schwartz, Tendler, and Vronman [1958].

11.2. Studies in Which the Radionuclide Is Injected Directly Into the Bloodstream

These tests are for the determination of

(a) Circulation time [Wright, Osborne, and Edmonds, 1949 and 1951].

(b) The passage of a radionuclide past the detector on the first circulation; for example, cardiac output [MacIntyre, Storaasli, Krieger, Pritchard, and Friedell, 1952], radiocardiography [Prinzmetal, Corday, Spritzler, and Flieg, 1949].

(c) Buildup of a radionuclide in a region; iodine accumulation in thyroid [Stanley and Astwood, 1947]; peripheral vascular studies, especially in extremities [Smith and Quimby, 1945; Friedell, Schaffner, Pickett, and Hummon, 1949].

(d) Buildup and subsequent clearance; liver function with rose bengal [Taplin, Meredith, Kade, Westover, Hanse, and Bennett, 1955]; kidney function with iodine-labeled diodrast [Taplin, Meredith, Kade, and Winter, 1956].

11.2.1. *Administered amounts.* The administered amounts for these procedures range from 10 to 200 μc, but should be as small as possible in order to minimize the dose to patients. Except for the determination of cardiac output, which requires a precision of ± 4 percent and should be made with care, a high degree of precision is often not necessary. When the results are required for the setting up of mathematical equations or electrical analogs, however, the highest degree of precision obtainable is usually desirable.

11.2.2. *Equipment.* All of these tests require essentially the same equipment (e.g., fig. 11.2–1). Suitable apparatus comprises a well shielded and (usually) well collimated scintillation counter, a fast ratemeter, and a strip chart recorder. The desired information is obtained from an analysis of the recording. The strip chart recorder should preferably be of the rectilinear type to permit easy interpretation. In some cases a digital printer and scaling circuit may be useful, but the intervals at which readings are taken must be considered in relation to the physiological system under study.

11.2.3. *Precautions.* Some precautions are necessary in conducting satisfactory measurements of this kind. For example, in (a) and (b) the volume injected should be small and the injection carried out rapidly, and in most cases careful positioning of the counter is important.

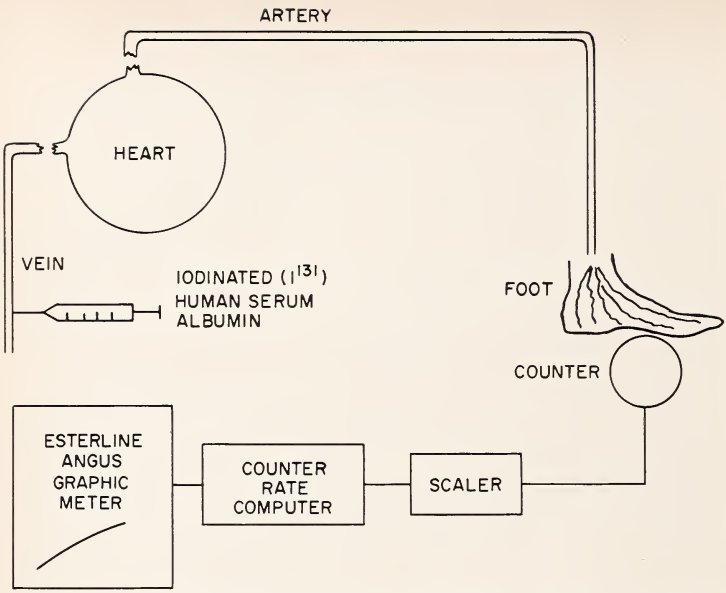


FIGURE 11.2-1. *Schematic diagram of experiment to measure peripheral vascular flow.*

MacIntyre, Storaasli, Krieger, Pritchard, and Friedel, 1952; courtesy of Radiology.]

11.3. Studies in Which the Radionuclide Is Injected Directly Into a Tissue

This type of study is undertaken for the determination of tissue "clearance" rates [Kety, 1952; Wisham and Yalow, 1952; Barron, Veall, and Arnott, 1951; Conway, Roswit, Stark, and Yalow, 1951].

11.3.1. *Administered amounts.* The amounts administered may be less than 1 μc and, because the measurements are relative, need not be known accurately. The quantity used must be within a suitable range and as small as possible to minimize the dose to the patient.

11.3.2. *Equipment.* The equipment is essentially the same as indicated above, although a small end-window Geiger-Müller counter and minute-by-minute counting may be employed.

11.3.3. *Precautions.* The precautions necessary include insuring that the window of the counting tube is not directly over the cutaneous entrance portal. In measuring clearance rate from a tissue below the skin surface, it is important to make sure that significant needle tract contamination in more

superficial tissue levels is not contributing unduly to the recorded count.

11.4. Background

If only a general qualitative picture is desired, the presence of a high, or even a changing, background may not be important. If a truly quantitative picture of variation of concentration with time is required, enough shielding must be used to keep background low. If a changing background (with change in distribution of the radionuclide in the body) influences the precision of the measurement, a spectrometer may be advantageous for supressing at least that part of the response due to scattered radiation (sec. 7.6).

12. Measurement of Postadministration Samples

12.1. General

Most clinical and biological procedures with radioactive materials involve the administration of this material to the system under test and the subsequent recovery of samples from the system for quantitative measurement, for distribution study, or sometimes for identification of the molecular form containing the radioactive material. Many of the measurements are relative to the amount administered and consequently, while the precision desired may be high, the accuracy required is generally not high. The achievement of precision is principally the result of consistency of technique in sample preparation, in geometry of both source and source detector arrangement and in measurement practices. Frequently a compromise must be effected between the time spent on the measurement and the degree of precision required. The magnitude of sample counting rate relative to background and statistical considerations thus become most important. These are discussed in section 2.5.2 and the practical applications are considered by Loevinger and Berman [1955].

The determination of the radionuclide distribution in cells by autoradiography or in molecular species by radio-paper-chromatography and paper electrophoresis is generally more qualitative and more limited in application, but in some cases is capable of considerable precision.

The sensitivity of the method of assay employed usually determines the amount of material that must be administered to the system. The most sensitive method of assay available should be used in order to minimize radiation effects on the system and to reduce the possibility of interfering with the normal physiological processes by, for example, unusually large amounts of the stable isotope.

Whenever feasible, it is advantageous to use the whole sample since this will contain the maximum amount of radioactivity and errors due to subsampling are avoided.

If subsampling is necessary, the portion taken should be representative of the material it is desired to measure. At least two subsamples and often many more should be taken from the same material, especially when dealing with difficult material such as bone.

Contamination of the sample with radioactivity from other sites, samples, sampling and injection equipment, containers, and so forth, must be avoided.

12.2.1. *Fresh specimens.* When weights of fresh specimens are necessary for concentration calculations, the samples should be weighed before any appreciable moisture loss has occurred. If they cannot be weighed immediately, they should be kept in closed containers to minimize weight loss. With some small samples such as adrenals, thyroids, or pituitaries of laboratory animals, it becomes almost impossible to obtain accurate fresh weights and it is usually better to express the results on a dry-weight basis. Samples should be dried as soon as possible after collection to minimize chemical and biological changes such as dry-weight losses due to respiration. The material should be dried in a well ventilated oven at 60 to 70° C, since good ventilation tends to reduce decomposition of organic constituents. In special cases, it may be necessary to dry under a vacuum. If dry weights are required, the samples should be finished at 100 to 110° C. If the dried material is hygroscopic, weighing bottles may be needed for the drying and weighing.

12.2.2. *Preparation of liquid samples.* Liquid samples of clinical and biological importance should be assayed as liquids whenever possible. It may be necessary in some cases to use an agent to prevent precipitation or separation of the components. Liquid assay should be conducted under conditions of constant geometry (which includes constancy of liquid volume).

Solid samples may in some instances be rendered suitable for assay as liquids by dissolving in an appropriate solvent. Solid samples of soft tissue may be considered as liquid (water) of equivalent mass providing the disposition of the sample relative to the measuring system is approximately the same as that of a similar liquid sample. Where adjustment to a fixed volume is either practically or esthetically undesirable (as, for example, in the measurement of feces

contained in a sealed carton), an adjustment in the weight of the calibrating sample may be an alternative. Some loss of accuracy is inevitable, but in many circumstances this may not be serious.

Bulky liquid or solid samples can sometimes be concentrated by evaporation or ashing, respectively, and then redissolved. Methods of wet ashing and dry ashing are described in detail in the literature [Piper, 1947; Comar, 1948, Middleton and Stuckley, 1953; Comar, 1955, ch. 5]. Some chemical separation may also be necessary to reduce the bulk of material. Care must be exercised to ensure that relevant radioactive material is not lost in the sample preparation procedure.

12.2.3. *Preparation of solid samples.* Solid samples which cannot be assayed as liquid should be rendered as uniform as possible in composition and may be assayed either as thick or thin samples.

12.2.31. *Thick samples.* This term is reserved for beta-emitting samples of thickness greater than the maximum beta range. The number of particles leaving the surface depends only on the specific activity per gram of sample (assuming constant geometry), and, by comparison with a suitable standard, self-absorption and similar corrections are avoided. Although the method is of greatly reduced efficiency compared with thin sample assay, it is very convenient and, if sufficient activity is present in the sample, it is usually the most reliable and satisfactory.

12.2.32. *Thin samples.* Thin samples usually result from deposition of a liquid aliquot on a planchette (usually metal) followed by evaporation. Evaporation is best carried out slowly on a hot plate or under an infrared lamp. Sputtering must be avoided. Wetting an area of the planchette with a wetting agent will often prove effective in providing a uniform deposit. The metal of the planchette may have to be varied according to the solution contents, and for this reason calibration should always take place with an identically prepared sample. In special circumstances, techniques such as electroplating may be necessary. It is important, particularly with low-energy beta particles, to keep the amount of solid material in the sample as low as possible to reduce the magnitude of self-absorption and self-scattering corrections. (For detailed discussion of self-absorption, see Comar, 1955, p. 177–183.)

12.2.4. *Preparation of gas samples.* For very low-energy beta emitters such as carbon-14 and hydrogen-3, gas samples prepared from liquid or solid samples are particularly useful.

This procedure generally involves the oxidation of carbon-14 to $C^{14}O_2$ and the reduction of hydrogen-3 to molecular hydrogen. Techniques for these procedures are described in the literature [Calvin, Heidelberger, Reid, Tolbert, and Yankwich, 1949; Glascock, 1954].

12.3. Calibration Techniques

In sample assay procedures, comparison is usually made with a known reference sample of the same radioactive material under identical and reproducible geometrical conditions. An aliquot of the actual injected material should be used as the reference sample whenever possible. Alternatively, the sample measurement may be related, by means of a long-lived performance standard, to a previous measurement involving a reference standard (in which the efficiency of the arrangement for the same radionuclide was determined) (sec. 7.7).

Whether or not direct comparison is made with an aliquot of the injected material, a performance standard should be used at least once on each day that assays are made.

If it is not practical to use samples of identical volume and weight, the sensitivity of the arrangement to changes in volume or weight must be accurately known. The method of identical geometry and volume is always to be preferred, however, since self-absorption and similar corrections are then unnecessary.

12.4. Gamma-Ray Sample Assay

12.4.1. *Small samples (up to 5 ml).* The most convenient and efficient method is to use a scintillation counter with a well-type sodium iodide crystal. If a standard glass vial is used as a sample container, accurately reproducible geometry is obtained and the efficiency is as high as can be obtained by any present method of gamma-ray counting (as high as 45 percent for gamma-ray emitters such as cobalt-60, iodine-131, and gold-198; the method is described in sec. 7.6). For very small samples, well counters of this kind can be used with some loss of sensitivity if the volume is made up to the standard volume used, although it may be preferable, for greater sensitivity, to use a crystal with a smaller well and sample vial. For very large samples the well counter may be used by taking aliquots but it may be preferable to measure the sample in bulk, by another method (sec. 12.4.2), particularly if the volume exceeds 100 ml.

The well-scintillation counter may also be used for the separation of radionuclides used in multiple tracer studies

(such as the separation of iron-59 and chromium-51). This can be accomplished by adding a pulse-height analyzer (usually single channel) to the electronic equipment, in order to restrict the selection of incoming gamma rays to a chosen range of energies of rather narrow width. This makes it possible, for example, to distinguish between radionuclides with different gamma-ray energies. Restricting the channel width reduces the efficiency of sample counting and also the background, and the ratio between sample and background *may* become more favorable (compare tables 7.6–1 and 7.6–2).

12.4.2. *Large samples.* With large samples it is no longer practical to use a well-type method since the surrounding sensitive medium becomes inconveniently large and difficulties of light collection considerable. Furthermore the background becomes objectionably high. Two alternative methods are:

12.4.21. *Method 1.* Representative of this method is an instrument with 6 long Geiger-Müller cylindrical counters arranged vertically in a circle to provide a well, inside which bottles of large volume can be placed. Such arrangements can be shown to have rather low sensitivity to changing volume when the volume is large and can readily measure amounts of the order of 1 μc of iodine-131 in volumes of the order of 2,000 or 3,000 ml. The minimum detectable amount of such an arrangement is often much smaller still—of the order of $\frac{1}{100}$ to $\frac{1}{1000}$ μc [Veall and Vetter, 1952].

12.4.22. *Method 2.* In this case the desirable geometry of the well is sacrificed and the large-volume bottle is placed over a sodium iodide or a large plastic scintillation crystal. Some increase in background is usually inevitable, but for volumes of about 1,000 ml the efficiency obtained may be about 1 or 2 percent for a well crystal. (The same crystal may have an efficiency of over 40 percent for iodine-131 or cobalt-60 for a volume of 4 ml placed in the well.) The net gain in sensitivity may nevertheless be considerable using such a method. The change in sensitivity with volume must be determined for each type of container used and for the individual arrangement. The efficiency may easily vary by a factor of 4 for volumes from 100 to 1,000 ml, but for most arrangements varies in very nearly the same manner for gamma rays from both iodine-131 and cobalt-60. A small change in background with sample volume will also take place which in some circumstances may be insignificant and can otherwise be corrected for by determining the background with an identical sample containing no radioactivity.

12.5.1. *Liquid samples.* Methods of directly assaying beta-particle liquid samples usually provide geometrical conditions which will enable scattering, self-absorption, and wall absorption to be controlled. Examples of this method are jacketed counters [Veall, 1948], dipping counters, and Marinelli beakers. These use a thin-wall Geiger-Müller counter which will accept beta particles above a certain energy, usually about 0.4 Mev. Variation in response from counter to counter is usually considerable and individual calibration is necessary [Rose and Emery, 1951]. Other techniques are available for high-energy beta emitters on the one hand, and low-energy beta emitters on the other.

High-energy beta emitters may be measured in a well-type scintillation counter, such as that described for gamma radiation (sec. 12.4.1), by counting *bremsstrahlung.* It is desirable to use sufficiently thick-walled glass vials or additional filtration provided by metal in order to exclude any beta radiation from entering the sensitive volume of the crystal. The efficiency depends markedly on the beta-ray energy and, with phosphorus-32 for example, may be of the order of 0.5 percent. With higher-energy beta emitters the efficiency will be greater [Loevinger and Feitelberg, 1955].

For very low-energy beta emitters one of the few satisfactory methods of directly measuring liquid samples is by means of the procedure known as formamide counting with a windowless flow counter (see sec. 5.4.1). The liquid radioactive sample is mixed with liquid formamide (this material will take up to 10 percent of an aqueous solution without causing a high vapor pressure), and a flow-proportional counter will still operate satisfactorily with the mixture within it. Since it is most convenient to use the liquid sample as a "thick" sample (sec. 12.2.31), the efficiency is not high (of the order of 1 percent for carbon-14) but the method is simple and reliable (see also sec. 4.3).

12.5.2. *Solid samples.* Solid samples may be prepared from liquid samples by evaporation (sec. 12.2.3) and placed either on sample planchettes or spread over a suitable geometrical configuration such as a cylinder. The relationship between sample and detector must be fixed and reproducible.

For samples on planchettes the detector may be an end-window type Geiger-Müller counter, a 2π proportional-flow counter or an anthracene or plastic scintillator with a thin window. This method is most suitable for higher energy beta emitters for which efficiencies of more than 30 percent are common.

Alternatively, the sample may be spread out over the inner surface of a cylinder and placed over a cylindrical gas-flow counter with thin mylar walls [Libby, 1957]. Higher efficiencies are possible and the method is suitable for a wide range of beta emitters.

Very low-energy beta emitters can be measured in a windowless flow counter, which may be either of the Geiger-Müller or proportional type.

If the sample is "thick," the number of beta particles emitted from the surface will be dependent only on the specific activity per gram of material, and self-absorption corrections are avoided if comparison is made with a reference source which is also "thick" (sec. 12.2.3). This method is very useful when the sensitivity is adequate.

If "thick" samples cannot be used, self-absorption and scattering resulting from the thickness of the sample material, which may differ from that of the calibration source, must be considered. In these circumstances it is desirable to keep the solid material in the sample as low as possible in order to have maximum sensitivity and minimum self-absorption correction. In many circumstances approximate methods for correction will suffice (see Comar, 1955, p. 177–183).

12.5.3. *Gas samples.* A method useful with very low-energy beta emitters is to convert the sample to gaseous form (sec. 12.2.3) and actually use it as, or mix it with, the gas of the counter or ionization chamber. High detection efficiency is thus possible, but the method is more elaborate than other methods of beta sample counting.

12.5.31. *Internal-gas-counting.* Internal-gas-counting techniques can be used in the case of any beta-emitting or electron-capturing nuclide that can readily be converted to a suitable gaseous compound. Thus carbon-14 assays may be carried out by converting the carbon residues or samples to carbon dioxide or even to acetylene or methane, but the preparations of the latter two compounds would be more difficult (see sec. 3.3).

12.5.32. *Ionization-chamber techniques.* Although ionization chambers are not usually as efficient as counters for most assay procedures, for low-energy beta counting, if a large sample is available more of it may be used effectively in an ionization chamber than in a gas counter. Counting techniques are usually suitable for amounts of less than 1 mM of carbon-14-labeled gas, whereas ionization chambers may measure samples of 10 mM or more. The ionization chambers used are generally quite large, 250 ml or more, and the voltages required are of the order of a hundred volts.

Currents of the order of 10^{-15} ampere are commonly measured with a vibrating-reed electrometer. The system is usually calibrated with a standard sample assayed by another method. The ionization-chamber system then has the advantages described in sec. 7.2 which are characteristic of all ionization-chamber systems, notably stability and reliability. Since in many biological systems the required size of sample can be made available, the ionization-chamber technique is rather widely used [Brownell and Lockhart, 1952].

12.5.4. *Liquid scintillation counting.* Liquid scintillation counting is a valuable method for very low-energy beta emitters, particularly hydrogen-3 and carbon-14. Solid samples are dissolved in a liquid luminescent medium or liquid samples are mixed with the luminescent medium. The sample-plus-detector liquid cell is usually placed between two photomultiplier tubes arranged in coincidence. Because of the very low pulse amplitudes obtainable it is necessary to cool the photomultiplier tubes (with CO_2 or liquid nitrogen) and thus obtain a favorable signal-to-noise ratio. With such an arrangement, efficiencies of the order of 50 percent for carbon-14 and of the order of 6 percent for hydrogen-3 are obtainable [Wagner and Guinn, 1955] (see also section 7.6.3).

12.6. Paper Chromatography and Paper Electrophoresis

Paper chromatography can greatly increase the effectiveness of radionuclide techniques. The primary usefulness of paper chromatography lies in the following: (a) Separation of mixtures into their constituents, (b) demonstration of homogeneity of chemical substances, (c) demonstration of identity of substances, and (d) quantitative or qualitative estimation of one or more substances present in a mixture. The method has become of particular value because a great many important biochemical compounds occur in nature as complex mixtures of substances of similar properties and structure, and are therefore most difficult to resolve by other means.

As a separation procedure, paper chromatography is highly efficient as compared with batch procedures. The sensitivity is high, the detection of the "spots" usually being the limiting factor; this is precisely where radioisotope techniques may offer considerable advantage. Another important feature is that the procedure is simple and rapid, requiring no equipment except filter paper, chemicals, and glassware, which is in contrast to other chemical separation

procedures such as fractional crystallization or distillation. Also, the latter procedures can be used only with substances that can be crystallized or distilled, and they often require elevated temperatures, which may degrade the test substance. Large numbers of samples can be analyzed by paper chromatography even with limited facilities. The procedure is carried out by the application of a small drop of test solution a short distance from one end of a strip of filter paper. After the drop has dried, this end of the strip is placed in an appropriate solvent so that the latter moves past the spot by capillary action and along the paper. This results in a differential movement of the components of the test solution along the paper. The solvent usually consists of a stationary aqueous phase which has a strong affinity for the filter paper, and an organic or mobile phase which tends to move along the paper. As the mixed solvent flows through the section of paper containing the test substances, the latter are distributed between the organic phase, which is moving rapidly ahead, and the stationary aqueous phase. After completion of the separation, the individual zones or spots are identified by color reactions, radioactivity, or other methods. Details can be found in a number of references.[4] In this section the discussion will be principally concerned with methods using radioactivity.

12.6.1. *Techniques of paper chromatography.* There are various general techniques of paper chromatography, each of which has certain advantages for specific purposes. These may be described as follows:

Descending chromatography
Ascending chromatography
Ascending-descending chromatography
Two-dimensional chromatography
Multiple development
Circular or horizontal filter-paper chromatography
Preparative paper chromatography.

Brief comment follows on some of the specific experimental techniques.

12.6.2. *Experimental considerations in paper chromatography.*

12.6.21. *Choice of filter paper.* Numerous commercial filter papers are satisfactory for chromatographic separations.

---

[4] Wilson, 1940; Zechmeister and Cholnoky, 1941; Strain, 1945; Weil and Williams, 1950; Cassidy, 1951; Toennies and Kolb, 1951; Williams, 1951; Strain and Murphy, 1952; Smith, O. C., 1953; Comar, 1955; Desty and Harbourn, 1957; Lederer and Lederer, 1957; Block, Durrum, and Zweig, 1958, Smith, I., 1958.

The best paper for any given experimental requirements and conditions would have to be determined by trial. Characteristics of importance include texture, uniformity, and solvent speed. Description of the suitability of specific papers can be found in the literature [Block, Durrum, and Zweig, 1958; Lederer and Lederer, 1957; Smith, I., 1958].

12.6.22. *Application of sample.* The application of the sample to the paper is quite simple and yet may be tedious when large numbers of chromatograms are involved. Usually 5-μl pipets are employed. If it is necessary to use larger amounts of solution, the paper should be dried after each 5-μl application. Larger pipets may be used if the sample can be continuously dried in a current of warm air. It the initial spot is too large (greater than about 1-cm diameter), the chromatogram tends to be diffuse and indefinite. Ingenious commercial equipment is available for uniform application of the small volumes to paper strips.

12.6.23. *Solvents.* Numerous specific solvent mixtures have been described [Block, Durrum, and Zweig, 1958; Lederer and Lederer, 1957; Smith, I., 1958]. In most solvent mixtures, the water is used to saturate the organic solvent and only the saturated organic phase is used on the chromatogram.

12.6.24. *Detection of spots.* If radioactive materials are being used, then the spots may be readily detected by counting procedures or autoradiography. Commercial automatic scanning devices are available; these are based upon a method of moving the paper strip slowly past a counter, with the counts being automatically recorded on a chart that can be matched against the chromatogram. By regulation of the rate of strip movement and the width of the slit between the paper and counter, the optimum measurement conditions can be attained. If non-radioactive materials are used, certain substances may be detected by virtue of their color or fluorescence. In general, however, it is necessary to use a reagent that reacts with the substances being separated to produce a visible color. If possible, the reagent should be applied in alcoholic solution, since this permits rapid drying and minimizes the spreading of spots. Usually the reagent is applied by light spraying. Specific color reagents have been described in the literature [Block, Durrum, and Zweig, 1958; Lederer and Lederer, 1957; Smith, I., 1958].

12.6.25. *Identification of spots.* A "map" can be prepared for the given experimental conditions using known compounds detected by chemical reagents, or known radioactive-labeled compounds. Also, the unknown radioactive

material may be chromatographed together with an authentic sample of the suspected substance. If the two compounds are identical, there should be complete coincidence of the spots due to the two substances.

12.6.3. *Quantitative estimation of separated substances by radioactive tracers.* Numerous methods have been suggested for the quantitative estimation of substances separated on the paper chromatogram, but when radioactive materials are used, the quantitative determination of amounts of substance present is greatly simplified. The method outlined in section 12.6.24 for the detection of spots may be sufficiently refined, especially when compared with similarly treated standards, to yield reliable quantitative results. Advantage may be taken of isotope-dilution procedures to avoid the time and trouble necessary for complete separations [Comar, 1955]. It is often found convenient to measure separated sections of the paper by conventional radiochemical and radioassay procedures. The inherent sensitivity of measurement of radionuclides offers considerable advantage.

The smallest activity necessary for a given determination depends on the fraction of the activity ultimately presented to the counter, and on the characteristics of the radionuclide and counting system.

The resolution required will determine the largest possible slit which can be used in the counter. The larger the acceptable slit, the larger will be the radioactive sample presented to the counter. The migration pattern of the tagged material may produce a narrow, high-activity band, so that a large sample will be presented to the counter with a given slit width; when a diffuse migration pattern occurs, the opposite effect will take place and the activity presented to the counter will be less.

Geiger-Müller-, proportional-, and scintillation-counting techniques can be used, with a count-rate meter for continuous recording. To obtain maximum resolution the time constant of the rate meter and speed of the paper strip past the counter have to be set appropriately for a given activity and for the time available.

Self-absorption will depend on the thickness of the paper. For the counting of soft beta emitters the thinnest paper should be used, but other requirements of the experiment may make a compromise necessary.

Recent techniques for paper-strip scanning involve impregnation of the paper with a scintillating phosphor [Seliger and Agranoff, 1959] or the immersion of the paper in a liquid scintillator [Roucayrol, Oberhausen, and Schubler, 1957].

12.6.4. *Quantitative estimation of separated substances by other methods.*

12.6.41. *Color comparison.* Since in certain chemical reactions the intensity of a color varies with the quantity of material present, it is possible to make estimates of the quantity of material present by visual comparison with known samples chromatographed in exactly the same way as the unknown. Difficulties arise on account of (a) lack of contrast between spot and background, (b) necessity of using an amount in the concentration range in which the visible gradation of color will be a function of concentration, and (c) interfering substances that may be present in the sample and not in the standard. The success of this method will be primarily dependent upon standardization of experimental conditions.

Various modifications have been employed using densitometers or colorimeters in an effort to determine the total color of the spot or the maximum color density and to relate these empirically to standard solutions. Commercial equipment, specifically designed for this purpose, is now available.

12.6.42. *Determination of spot area.* It has been shown that usually the logarithm of the area of a spot is a linear function of the concentration. The area can be experimentally determined by use of a planimeter or by cutting out the spot and weighing the paper. The area method is usually less sensitive than the color-comparison method but is less affected by experimental variables. It can be used only where the boundaries are distinct, and in any event standards are required.

12.6.43. *Elution.* Of most general application, perhaps, is the procedure of cutting out the spot of the chromatogram containing the separated material, dissolving the material from the paper, and analyzing it by the appropriate method. The limiting factor will usually be the sensitivity of the analytical method.

12.6.5. *Paper electrophoresis.* Paper electrophoresis is based on the differential migration of solutes due to application of an electrical current. Paper electrophoresis can be utilized with or without simultaneous chromatographic separation. Over 2,000 papers on this subject have now been published and from standard texts equipment may be chosen for any given problem [Comar, 1955]. Although there are numerous minor modifications of instrumentation, the basic techniques of paper electrophoresis can be classified as follows:

1. Closed strip (evaporation prevented)
   (a) Solid support
   (b) Nonpolar liquid
2. Semiclosed (evaporation permitted)
3. Open strip (evaporation permitted)
   (a) Horizontal type
   (b) Hanging-strip type.

Attention is called to equipment now commercially available that operates on the continuous-flow principle. Some advantages are as follows: (a) Relatively large amounts of materials can be separated, (b) difficulties due to absorption by the filter paper are minimized, (c) the choice of solvent or background electrolyte is not as critical as in conventional paper electrophoresis, and (d) no cutting up and elution of paper are required, since the fractions are collected off drip points.

12.7. Autoradiography

Autoradiography permits visualization of the location of radioactive nuclides within a sample. The technique is of particular advantage with heterogeneous samples in providing information that is unobtainable by counting methods. Applications range from the micro scale, which permits study of individual subcellular elements, to the gross scale, which, for example, is useful for evaluation of macrodeposition in tissues and paper chromatograms.

Autoradiography does not generally require electronic equipment; much the same art and science will be required for meaningful results as are needed for conventional histochemical techniques. Adequate references are available that cover aspects of methodology and application [Yagoda, 1949; Gross, Bogoroch, Nadler, and Leblond, 1951; Heller, 1951; Herz, 1951; Leblond and Gross, 1951; Bourne, 1952; Fitzgerald, 1952; Fitzgerald, Simmel, Weinstein, and Martin, 1953; Boyd, 1955; Comar, 1955].

The techniques require consideration of the following subjects: photographic emulsion, relevant properties of the radionuclide, amount of radionuclide and exposure time, handling of tissues, photographic processing, staining, and evaluation.

12.7.1. *Autoradiographic procedures.* There are four commonly used procedures that differ primarily in the method of contact between tissue section and emulsion. A brief statement of the principle, advantages, disadvantages, and recommended use is presented for each.

12.7.11. *Simple apposition.* Principle: The specimen to be studied is placed in contact with the photographic

emulsion and kept in contact by pressure; at the end of the exposure period the specimen is removed, and the film developed.

Advantages: The method is rapid and simple, and pretreatment of the sample is minimal, so that radionuclide losses are avoided. Since poor resolution is inevitable, it is possible to make advantageous use of a sensitive film to decrease the exposure time and/or the amount of radioactivity required in the sample. The autoradiogram can be used for densitometric measurement, since there will be no interference from the specimen. The sections can be stained after preparation of the autoradiogram, and there is no interference from the emulsion.

Disadvantages: Poor contact is responsible for loss of resolution, and cellular localization is usually not possible. It is difficult to superimpose accurately the object and autoradiogram.

Recommended use: This method is satisfactory for gross autoradiograms, especially for samples in which the radionuclide localizations are widely separated. It has been particularly useful in studies with bones, frozen tissue, and paper chromatograms.

12.7.12. *Mounting method.* In this method, which is illustrated in figure 12.7–1, the sections are mounted on the emulsion and remain permanently bonded thereto throughout the subsequent photographic and staining processes.

Advantages: The method is relatively simple. The contact, registry, and resolution are good, thus permitting studies on the cellular level. The autoradiogram and section are always matched and are observed simultaneously; this allows correlation between structure and photographic image.

Disadvantages: There are possibilities of radionuclide loss during the fixation and processing of the tissue. There may be spotty development on account of nonuniform penetration of the tissue by the developer. The emulsion gelatin tends to absorb the tissue stain, and also the photographic darkening may be masked by the opacity of the tissue. There is the possibility of chemical effects on the emulsion due to direct contact with the tissue. This technique is difficult to use with plastic or celloidin-embedded material.

Recommended use: The mounting method has been widely used for iodine-131 localization in thyroid tissue. Also, blood smears and bone-marrow smears have been studied by applying such samples directly to the surface of the emulsion.

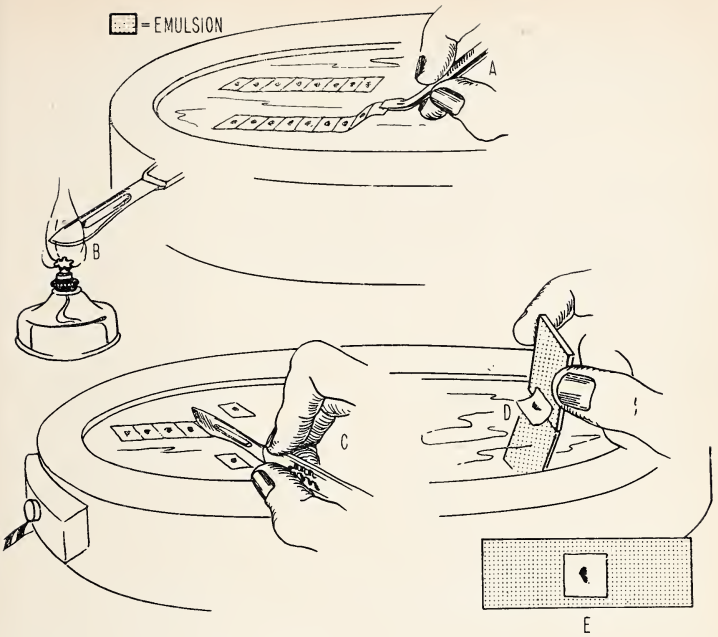


FIGURE 12.7–1. *Mounting method.*

Cut tissue sections are floated on warm water to remove the wrinkles (A), a knife blade heated (B), the sections separated from the ribbon (C), and the sections picked up by placing the photographic plate in the water beneath them (D) to obtain the permanently mounted section shown at (E). [Fitzgerald, Simmel, Weinstein, and Martin, 1953; courtesy of Paul B. Hoeber, Inc.].

12.7.13. *Coating method.* In this method, which is illustrated in figure 12.7–2, the section is covered with a fluid emulsion which is allowed to harden and forms a permanent bond for subsequent exposure and processing.

Advantages: Good contact and constant registry are obtained which lead to good resolution and allow good correlation of radioactivity with histological structure, since the photographic image and section are observed simultaneously. A celloidin layer protects the tissue from photographic processing fluids, and in the inversion method [Comar, 1955], the photographic image is protected from staining fluids. The thickness of the fluid emulsion can be somewhat controlled.

Disadvantages: The handling of the emulsion tends to increase the background fog, and the preparation of an emulsion of uniform thickness is difficult. There are

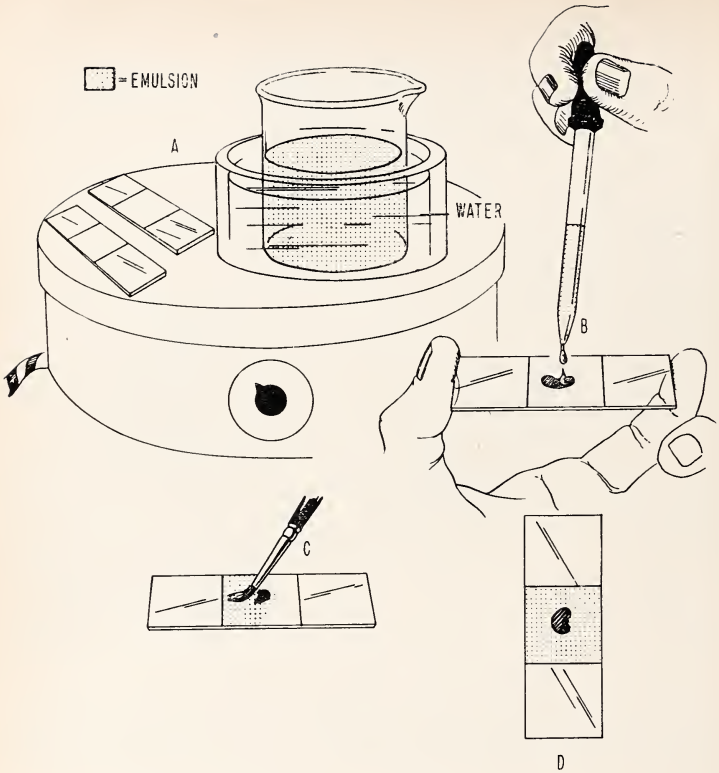


FIGURE 12.7–2. *Coating method.*

The gel is maintained at 37 °C in a beaker, and the slides are warmed (A); drops of the fluid emulsion are applied to specimen on marked slide (B); the drops are spread evenly (C); and the slide is tilted to give even distribution (D). [Fitzgerald, Simmel, Weinstein, and Martin, 1953; courtesy of Paul B. Hoeber, Inc.]

possibilities of radionuclide loss during any preliminary histological processing and also by solution into the liquid emulsion.

Recommended use: Coating autoradiograms have proved satisfactory for cytological studies with bones, teeth, and soft tissues.

12.7.14. *Stripping-film method.* In this method, which is illustrated in figure 12.7–3, an emulsion is stripped from its base and flattened over the histological section or smear on a glass slide. The specimen can be stained either before contact with the film or through the film base after exposure. Unstained sections can be studied by phase microscopy.

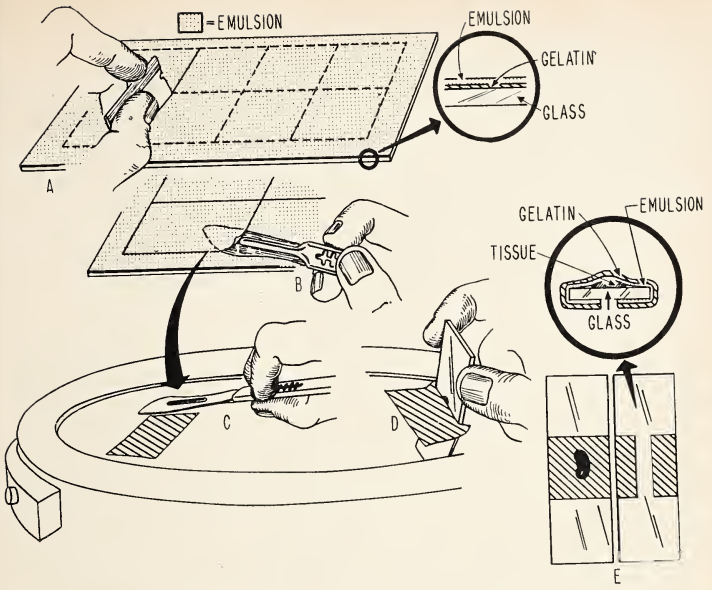


FIGURE 12.7–3. *Stripping-film method.*

The film is cut, as at (A); removed, as in (B); inverted and floated on water, as shown at (C); and picked up on the mounted specimen, as shown at (D). The film is draped around the slide to make a tight fit, as in (E). [Fitzgerald, Simmel, Weinstein, and Martin, 1953; courtesy of Paul B. Hoeber, Inc.]

Advantages: The procedure is somewhat less tedious than the coating method; offers the advantages of even emulsion thickness, good contact, constant registry, and excellent resolution; and permits good correlation of radioactivity with histological structure. Depending upon the method used, the impervious base emulsion may protect the sensitive emulsion from the tissue.

Disadvantages: There are possibilities of radionuclide loss during the wet processing. The sensitivity is relatively low, and the base emulsion may interfere with staining and tend to reduce the resolution.

Recommended use: The stripping-film method has proved satisfactory for cytological studies with both plant and animal tissues. Quantitative results at low levels of activity have been made possible by the counting of grains.

12.7.2. *Sources of error in autoradiograms.* There are many possible sources of error in autoradiograms, and the following list should be kept in mind when translating the black specks of the photographic image into meaningful information:

1. Removal or relocation of the radioactive atoms by biological or physical processes during the time between sampling and formation of the photographic image.

2. Extraneous sources of image production, such as chemically active substances in the specimen; pressure on the emulsion; radioactivity in the films, chemicals, or glass used in processing; and stray light or ionizing radiation.

3. Fading of the latent image or desensitization of the emulsion by the specimen.

4. Nonuniform development.

5. Scratches in the film, deposition of debris.

6. Effects of staining solution on the emulsion.

7. Movement of sample on film during exposure.

Many of the uncertainties have been eliminated in the procedures that have been referred to. However it is always wise, when making a series of autoradiograms, to include similar samples with no radioactivity as a control for errors that may tend to produce extraneous images. With gross samples, it is sometimes possible to dissect out regions corresponding to different areas of darkening and measure the radioactivity.

Information on types of film suitable for particular purposes, their sensitivity, resolution and background, is summarized in table 12.7–1.

12.7.3. *Quantitative estimation with autoradiograms.* Autoradiography is used principally to obtain qualitative information on the distribution of radioactivity in biological material. However, it can also provide quantitative information regarding the actual activity deposited in particular regions. For this purpose the photographic density of the region on the autoradiogram is determined with a densitometer (using a sufficiently small aperture so that the density is uniform over the region viewed by the detector) and related to activity by a calibration curve for the film exposed to known activities of the radionuclide in question under identical conditions.

Autoradiograms may also be used to determine the radiation dose, in rads, delivered to particular regions of tissue by exposing the film to a "block" or thick section of the tissue under precisely controlled conditions. The maximum and minimum dose in small regions may be found by using a small-aperture densitometer and comparing with calibration film exposed to known doses from the same radionuclide under the same conditions. The average dose in a large region of tissue may also be found by comparing the average attenuation by the film of a broad, uniform light beam with the attenuation of this beam through suitable calibration

TABLE 12.7-1. *Typical films for autoradiography*

Use	Type	Sensitivity	Resolution	Background
Gross localization or minimal concentrations.	No-screen X ray.	High	Poor	High.
Histological sections of moderate concentrations.	Medium lantern slide.	Medium	Good	Medium.
Histological sections that are mounted.	NTB	Medium	Very good	Low.
When β tracks are to be observed.	NTB_3	High for β tracks.	Very good	Increases rapidly.
When α tracks are to be observed.	NTA	High for α tracks.	Very good	Low.
When tracks are to be observed.	Liquid emulsion.	High	Very good	Increases rapidly.
Cellular localization	Stripping film	Low	Very good	Low.

films. This technique has been applied to radiation dose determinations in the thyroid gland [Sinclair, Abbatt, Farran, Harriss, and Lamerton, 1956] and could be applied to many other biological situations. (For a series of references on autoradiography, note Laboratory Investigation 8, No. 1, Jan.–Feb. 1959, "Report on International Conference on Autoradiography, 1958.")

Part III. Disposal of Radioactive Materials

13. Disposal Procedure

13.1. Disposal Limits

It is not the purpose of this handbook to set disposal limits, but to refer the reader to the sources of such limits, to summarize them, and to present methods for determining quantities conforming to these limits.

Disposal levels have been suggested in various handbooks published by the National Bureau of Standards (NCRP-NBS Handbooks 49, 53, and 69, and the reader is also referred to NCRP–NBS Handbooks 48, 58, 65, and the forthcoming revision of Handbook 42, all dealing with allied subjects).

The regulations governing radionuclide disposal are, however, established by the Atomic Energy Commission and are contained in the Federal Register, title 10, CFR, part 20.301–305, and these regulations will form the basis of

this section. It should be pointed out that the reference cited quotes the regulations in force at the time of writing this Manual. Changes and revisions are to be expected in later regulations.

13.1.1. *Methods of disposal.* According to the provisions of the Federal Register, title 10, CFR, part 20.301–304, disposal may take place in the following ways:

13.1.10. *Transfer to authorized recipient.* I.e., to licensed commercial waste disposal agency, as provided for in the Federal Register, title 10, CFR, part 20.301.[5]

13.1.11. *In sanitary sewer systems.* The radioactive material must be readily soluble and dispersible in water and must not exceed

1. Per day: (a) The quantity which, when diluted by the average daily quantity of fluid released into the sewer by the licensee will result in an average concentration not greater than the values specified in appendix B, table I, column 2, of 10 CFR 20, or (b) 10 times the values quoted in appendix C of 10 CFR 20. The larger of (a) or (b) is permissible.

2. Per month: The quantity which, when diluted by the average monthly quantity of fluid released into the sewer by the licensee will result in an average concentration not greater than the values quoted in appendix B, table II, column 2, of 10 CFR 20.

3. Per year: Not more than 1 curie of all radioactive material per licensee.

4. Excreta from individuals undergoing medical diagnosis or therapy with radioactive material is *exempt* from these provisions.

13.1.12. *By burial in the soil.* This method may be used provided

1. The amount per burial does not exceed 1,000 times the amounts in appendix C of 10 CFR 20.

2. Burial is at minimum depth of 4 ft.

3. Burials are spaced not less than 6 ft apart.

4. Burials are limited to 12 per year in any one area. Larger amounts may be approved on application to the Atomic Energy Commission, supplying full details.

13.1.13. *Other methods.* Disposal by any other method than in sections 13.1.10. to 13.1.12. *may* be approved on application to the Atomic Energy Commission, supplying full details of the method and concentrations in air and water resulting from the disposal, pursuant to 10 CFR 20, 103 and 302.

---

[5] Referred to hereinafter as 10 CFR 20.

In the case of incineration, the air in the effluent from the stack must not cause any person to be exposed to average concentrations greater than the limits in appendix B, table II, column 1, of 10 CFR 20.

Residue from incineration shall be treated as other solid waste and must come under section 13.1.12. unless an alternative method is approved.

13.2. Determination of Permissible Disposable Quantity

13.2.1. *Liquid wastes.* The appropriate water flow must be known. For hospitals this may be based, on the number of beds, taking the flow as 1,000 liters per bed per day. For other institutions, the flow may be taken as 500 liters per person per day, or 0.5×10^6 ml per person per day. A hospital population is generally about twice the number of beds.

To obtain the permissible daily discharge, multiply the permissible water concentration for the radionuclide in question (app. B, table I, col. 2, of 10 CFR 20) by $0.5\times10^6\times$number of persons employed. This gives the permissible *daily* discharge of each radionuclide.

To obtain the monthly discharge, multiply the permissible water concentration for the radionuclide in question (app. B, table I, col. 2, of 10 CFR 20) by $0.5\times10^6\times30\times$ number of persons employed. This gives the permissible *monthly* discharge of each radionuclide.

Estimate the total output for a year on the basis outlined above, and if the amounts total more than 1 curie for all materials the permissible discharge levels must be reduced accordingly.

13.2.11. As an example, an institution of 100 persons receiving iodine-131, phosphorus-32, gold-198, and carbon-14 for its research program would be able to dispose of, individually, per month neglecting, for the moment, the one-curie per year limit.

I–131	$100\times10^6\times0.5\times30\times9\times10^{-5}$ $=13.5\times10^4\mu c=135$ mc
P–32	$100\times10^6\times0.5\times30\times6\times10^{-4}$ $=90\times10^4\mu c=900$ mc
Au–198	$100\times10^6\times0.5\times30\times9\times10^{-3}$ $=1350\times10^4\mu c=13{,}500$ mc
C–14	$100\times10^6\times0.5\times30\times10^{-2}$ $=1.5\times10^7\mu c=15$ c

Obviously these numbers are not realistic in that it is highly unlikely that such an institution would even buy such quantities of any of these nuclides, except possibly iodine-131, let alone dispose of them. Except in the case of a

major spill, it is probable that disposals of gold-198 and phosphorus-32 would rarely reach even 1 percent of the above values; for carbon-14 the possibility would be very much less.

It appears that iodine-131 is the only nuclide which might present a problem. If, in the institution in question, an average of 200 mc of this material were used in therapy each month (an unlikely circumstance for such a small institution), it is possible that half or more may be excreted in the patients' urine. Although the Federal Register (10 CFR 20.303) specifically exempts patients' excreta from its restrictions, it is felt that it would be preferable to include this disposal in the institutional average when practicable. If the amount of radionuclide is such that the quantity to be disposed of is greater than the permissible disposable amount, the more active samples may be stored for partial decay. This can be done conveniently by discriminating between the excreta of patients given large therapeutic doses and that from patients given smaller therapeutic or diagnostic doses. It should be noted also that some patients will be treated as outpatients and that the disposal of active excreta may not take place through the hospital sewer system.

From the point of view of the permissible disposal quantity of all radionuclides of 1 curie per year, since iodine-131 is the only nuclide having significant disposal quantities, it might be considered that 500 mc could be the annual quota for this material; this might represent 50 percent of the amount used in the institution. With a standing order of 200 mc per month, and an average delay of 5 days between shipment and disposal, an average 50 percent disposal quantity would be about 65 mc; this would be about 800 mc annually. One week's storage of the most active specimens could readily reduce this well below the necessary level.

It is repeated that this is an unlikely situation for such a small institution; for a larger institution the permissible disposable quantity increases in proportion to the number of persons, as far as concentration in the liquid effluent is concerned, but the 1-curie-per-year limitation still applies and would probably be the principal limiting factor.

13.2.12. For known volumes of disposable liquids, activities may be measured by any of the methods described in previous sections (see sec. 12).

For pipet and other glassware washings, it is reasonable to assume that not more than 1 percent of the purchased radionuclide will be thus squandered.

For wet waste resulting from mop-up of a spill, an estimate can be made from the known magnitude of the spill.

13.2.2. *Dry waste for incinerator.* Incineration shall be specifically approved by the Atomic Energy Commission pursuant to 10 CFR 20.302. The airflow in the institutional incinerator must be known (the institutional engineer can usually provide this information). This is usually obtainable from the pounds of waste incinerated per hour, since one pound of combustible waste will produce approximately 7,000 liters of gas. Allowance may be made for dilution due to auxiliary fuel, excess air and dilution after the gases leave the stack (see NCRP–NBS Handbook 53).

It must be known whether the radionuclide in question will vaporize or remain in the ashes, or whether significant dust-particle dispersion may occur. Representative information is contained in "Radiation Hygiene Handbook" [Blatz, 1959, pp. 21–54].

For those wastes which vaporize, analogous procedures to those outlined above, shall be followed using appropriate air dilution factors and appendix B, table II, column 1, of 10 CFR 20.

13.2.3. *Dry waste for disposal into environment* (trash or garbage, including ashes). This method may be used only if specifically approved by the Atomic Energy Commission and if the provisions of 10 CFR 20, 102 and 103 apply. Levels for such disposal appear in the National Committee on Radiation Protection and Measurements—National Bureau of Standards Handbooks, but each type of event must be an individual problem. In some cases permanent storage pits are used. Accurate records of all amounts disposed of in this fashion must be kept.

13.3. Measurement of Disposal Amounts

Although calculations of the average disposal rate are frequently the most useful manner of dealing with disposal problems, individual measurements are sometimes essential. This is usually the case whenever a sample of unknown origin is to be disposed of. Such unknowns occur from time to time owing to the data and labels on storage samples, for example, having been lost, or as the result of accidents or contamination providing waste of uncertain activity.

13.3.1. *Gamma-ray samples.* Gamma-ray samples of this type can be measured very adequately with suitable calibrated instruments of the survey type. The usual procedure is to measure the dose rate at a chosen distance from the

sample and thus estimate the activity. The method is essentially that of section 3.6, but more approximate procedures are adequate and an accuracy of ± 25 percent may be considered satisfactory.

13.3.2. *Beta-particle samples.* If the waste sample emits beta particles only, the previous method cannot be used. The most useful method is to use a survey instrument of the end-window Geiger-Müller-counter type and test various parts of the sample. The material may be disposed of by one of the recognized methods above, provided the levels do not exceed acceptable contamination levels (NCRP–NBS Handbook 48): (radionuclides such as carbon-14, sodium-22, phosphorus-32, sulfur-35, iron-59, cobalt-60, iodine-131, cesium-barium-137, gold-198—1,000 counts per minute uncovered very close to the window of a counter with a 2-square-in. window; radionuclides such as calcium-45, iron-55, strontium-yttrium-90—100 counts per minute on end-window Geiger-Müller counter, 2-square-in. window). Higher activities should either be stored to decay further, or an actual estimate must be made of the activity in the sample.

Appendix A

Nuclear decay data for radionuclides which may be useful in medicine [a]

Element	Z	Half-life	Radiation emitted	β Energies—Mev (number per disintegration) (EC K_α-X-ray listed with β)	$\overline{E}_\beta$ Mev/dis.	Annihilation radiation Mev	γ Energies—Mev (photons per disintegration)	Γ r-cm²/mc-h
Antimony-124	51	60 d	β^-, γ	2.31(0.23), 1.66(0.02) 1.59(0.07), 0.95(0.06) 0.61(0.51), 0.22(0.11)	0.35		2.11(0.07), 1.61(0.46) 1.45(0.02), 1.37(0.11) 1.33(0.02), 1.05(0.02) 0.97(0.03), 0.72(0.14) 0.64(0.07), 0.60(0.98)	9.8_2
Arsenic-76	33	26.5 h	β^-, γ	2.97(0.55), 2.41(0.32) 1.76(0.04), 1.20(0.07) 0.56(0.01), 0.33(0.01)	1.14		2.06(0.01), 1.22(0.06) 0.65(0.07), 0.56(0.05) 0.55(0.40)	2.1_8
Bromine-82	35	35.7 h	β^-, γ	0.44(1)	0.150		1.47(0.17), 1.32(0.27) 1.04(0.28), 0.83(0.25) 0.78(0.83), 0.70(0.28) 0.62(0.42), 0.55(0.75) 0.35(0.03), 0.25(0.06)	14.6_4
Calcium-45	20	164 d	β^-	0.25(1)	0.076			
Carbon-11	6	20.4 m	β^+	0.97(1)	0.380	0.511(2)		5.9_0
Carbon-14	6	5770 y	β^-	0.16(1)	0.050			
Cesium-134	55	2.2 y	β^-, γ	0.89(0.01), 0.65(0.75) 0.28(0.03), 0.09(0.20)	0.116		1.37(0.03), 1.31(0.01) 1.17(0.03), 0.80(0.08) 0.79(0.85), 0.60(0.97) 0.57(0.10), 0.56(0.12) 0.47(0.02), 0.20(0.10)	8.6_3
Cesium-137	55	30 y	β^-	1.18(0.08), 0.51(0.92)	0.23			
(92% to barium-137^m)	56	2.6 m	γ				0.66(0.81)	3.0_8
Chlorine-38	17	37.3 m	β^-, γ	4.81(0.53), 2.77(0.16) 1.11(0.31)	1.50		2.15(0.57), 1.60(0.43)	8.8_0
Chromium-51	24	27.8 d	EC, γ	[0.0049(1)]			0.32(0.10)	0.1_8

See footnotes at end of table, p. 140.

Nuclear decay data for radionuclides which may be useful in medicine [a]—Continued

Element	Z	Half-life	Radiation emitted	β Energies—Mev (number per disintegration) (EC Kα-X-ray listed with β)	$\overline{E_\beta}$ Mev/dis.	Annihilation radiation Mev	γ Energies—Mev (photons per disintegration)	Γ r-cm^2/mc-h
Cobalt-57	27	270 d	EC, γ	[0.0064(1)]			0.14(0.06), 0.12(0.92) 0.01(0.09)	[b] 0.9_1
Cobalt-58	27	71 d	EC, β^+ γ	0.47(0.15)[0.0064(0.85)]	0.035	0.511(0.30)	0.81(1)	5.4_4
Cobalt-60	27	5.2 y	β^-, γ	0.31(1)	0.094		1.33(1), 1.17(1)	12.9_6
Copper-64	29	12.8 h	EC, β^+ β^-, γ	0.57(0.38), 0.66(0.19) [0.0075(0.42)]	0.13	0.511(0.38)	1.34(0.01)	1.1_9
Gallium-72	31	14.3 h	β^-, γ	3.17(0.05), 2.5(0.05) 1.94(0.07), 1.51(0.07) 0.96(0.35), 0.68(0.24) 0.66(0.17)	0.357		2.51(0.19), 2.49(0.11) 2.20(0.32), 1.86(0.06) 1.68(0.02), 1.60(0.06) 1.46(0.04), 1.27(0.02) 1.23(0.01), 1.05(0.07) 0.89(0.11), 0.84(0.96) 0.81(0.03), 0.73(0.04) 0.63(0.23), 0.60(0.08) 0.44(0.01)	14.7_4
Gold-198	79	2.69 d	β^-, γ	0.96(0.99), 0.28(0.01)	0.328		0.68(0.01), 0.41(0.95)	2.2_7
Hydrogen-3	1	12.26 y	β^-	0.02(1)	0.006			
Iodine-125	53	60 d	EC, γ	[0.027(1)]			0.04(0.07)	[c] 0.0_4
Iodine-130	53	12.6 h	β^-, γ	1.02(0.46), 0.60(0.54)	0.285		1.15(0.31), 0.74(0.69) 0.66(1), 0.53(1) 0.41(0.23)	12.1_6
Iodine-131	53	8.05 d	β^-, γ	0.81(0.01), 0.61(0.87) 0.34(0.09), 0.25(0.03)	0.188		0.72(0.03), 0.64(0.09) 0.51(0.01), 0.36(0.80) 0.28(0.05), 0.08(0.02)	2.2_0

Iodine-132	53	2.33 h	β^-, γ	2.12(0.18), 1.53(0.24) 1.16(0.23), 1.0(0.20) 0.7(0.15)	0.49		2.2(0.02), 1.9(0.04) 1.40(0.13), 1.16(0.10) 0.96(0.23), 0.78(0.94) 0.67(1), 0.62(0.06) 0.53(0.28)	12.3[3]
Iron-55	26	2.7 y	EC	[0.0059(1)]				
Iron-59	26	45 d	β^-, γ	0.46(0.53), 0.27(0.46) 0.13(0.01)	0.118		1.29(0.43), 1.10(0.57) 0.19(0.03)	6.2[4]
Manganese-52	25	5.7 d	EC, β^+, γ	0.58(0.33) [0.0054(0.65)]	0.072	0.511(0.66)	1.45(1), 0.94(1) 0.73(1)	18.5[2]
Manganese-54	25	320 d	EC, γ	[0.0054(1)]			0.84(1)	4.7[0]
Mercury-197	80	2.7 d	EC, γ	[0.068(1)]			0.08(0.19)	[d] 0.07[0]
Mercury-203	80	47 d	β^-, γ	0.21(1)	0.10		0.28(0.31)	0.4[8]
Phosphorus-32	15	14.2 d	β^-	1.71(1)	0.70			
Potassium-42	19	12.4 h	β^-, γ	3.54(0.81), 1.98(0.18)	1.42		1.53(0.18)	1.3[6]
Radium-226 (In equilibrium with its gamma-emitting decay products)	88	1620 y	α, β^-, γ	Many			Many	[e] 8.25
Silver-111	47	7.5 d	β^-, γ	1.06(0.93), 0.81(0.01) 0.73(0.06)	0.34		0.34(0.06), 0.25(0.01)	0.1[3]
Sodium-22	11	2.6 y	EC, β^+, γ	0.54(0.90) [0.001(0.10)]	0.19	0.511(1.80)	1.28(1)	11.9[1]
Sodium-24	11	15 h	β^-, γ	1.39(1)	0.56		2.75(1), 1.37(1)	18.2[3]
Strontium-89	38	54 d	β^-	1.46(1)	0.56			
Strontium-90 with Yttrium-90	38 39	28 y	β^-	0.54(1) and 2.23(1)	0.19 and 0.93			
Sulfur-35	16	87.1 d	β^-	0.17(1)	0.049			

See footnotes at end of table, p. 140.

Nuclear decay data for radionuclides which may be useful in medicine[a]—Continued.

Element	Z	Half-life	Radiation emitted	β Energies—Mev (number per disintegration) (EC Kα-X-ray listed with β)	$\overline{E_\beta}$ Mev/dis.	Annihilation radiation Mev	γ Energies—Mev (photons per disintegration)	Γ r-cm²/mc-h
Tellurium-121	52	17 d	EC, γ	[0.026(1)]			0.58(0.87), 0.51(0.13) 0.07(0.02)	[f] 3.3₀
Tin-113	50	118 d	EC, γ	[0.024(1)]			0.26(0.02)	[g] 1.5₀
(decays to indium-113[m])	49	1.7 h	γ				0.39(0.65)	
Yttrium-90	39	64 h	β^-	2.23(1)	0.93			
Zinc-65	30	244 d	EC, β^+, γ	0.32(0.02) [0.008(0.98)]	0.0024	0.511(0.03)	1.11(0.49)	2.9₀

[a] In this table are listed most of the radionuclides currently used in medical practice or research. The nuclear data represent a collection from a number of published sources, but the great majority has been kindly supplied by C. I. McGinnis of the National Academy of Sciences-National Research Council Nuclear Data Group. The bromine-82 gamma-ray data are from unpublished information supplied by private communication by A. H. W. Aten for the ICRU Committee I (1959) Report. Only beta and gamma rays with an intensity of 1 percent or more are listed and their energies are given to the nearest 0.01 Mev. Intensities are given to the nearest 1 percent. Auger and conversion electrons have not been included in the average beta-ray energies of col. 6. In the case of electron capturers, K_α-X-ray energies and the number of electron captures per disintegration have been given in square brackets in col. 5, but neither these X rays nor the X rays arising from conversion electrons have been included in the calculation of Γ, which is defined for gamma rays only. The gamma-ray intensities in col. 8 are those for photons only and do not include the intensities of conversion electrons. The values of Γ were computed by W. B. Mann, using a dose-rate-photon-energy curve calculated by K. W. Geiger from the data given in table 8-1 of the 1959 ICRU Report for a value of W=34.0 ev per ion pair.

[b] If the 6.4-kev K_α-X-ray, arising from electron capture, were treated as a gamma ray, then the value of Γ would be 7.4 r cm²/mc-h and the inclusion of such X rays arising from internal conversion of the 14.4-kev gamma ray (which in all other cases, except tin-113 and iodine-125, make a negligible contribution) would increase the value of Γ to 12.5 r-cm²/mc-h. The data used in this and following footnotes to calculate the ratio of K to L electron capture were obtained from Brysk and Rose (1958).

[c] If the 27-kev K_α-X-ray, arising from electron capture, were treated as a gamma ray, then the value of Γ would be 0.7 r-cm²/mc-h and the inclusion of such X rays arising from internal conversion of the 35-kev gamma ray would increase the value of Γ to 1.4 r-cm²/mc-h.

[d] If the 68-kev K_α-X-ray, arising from electron capture, were treated as a gamma ray, then the value of Γ would be 0.35 r-cm²/mc-h.

[e] r-cm²/mg-h; 0.5-mm Pt filter.

[f] If the 26-kev K_α-X-ray, arising from electron capture, were treated as a gamma ray, then the value of Γ would be 4.2 r-cm²/mc-h.

[g] This value of Γ is for tin-113 in equilibrium with indium-113[m], their respective contributions to Γ being 0.03 and 1.47 r-cm²/mc-h. If the 24-kev K_α-X-ray arising from electron capture, were to be treated as a gamma ray, then the equilibrium value of Γ would be 2.5 r-cm²/mc-h and the inclusion of such X rays arising from internal conversion of the 0.39-Mev gamma ray would increase the value of Γ to 2.8 r-cm²/mc-h.

Appendix B

Preferred methods of measurement for clinical and biological purposes

Class	Purpose	Radiation	Type	Approximate sensitivity	Remarks
I Pre-administration measurement	Calibration of shipments or aliquots.	β, γ or *bremsstrahlung*.	Calibrated well ionization chamber.	1 μg radium up	One standard design available is that of NPL. (see table 7.2–1).
	Checking of aliquots for administration.	γ and *bremsstrahlung*.	Simple fixed geometry Geiger-Müller or scintillation system.	0.1 μc up	If previous measurement of shipment is made, accuracy required is not high.
	Measurement of dose rate from small sealed sources.	γ	Ionization chamber and fixed geometry.	Usually of order of 0.1 mc up.	Various systems exist. Necessary for therapeutic situations where dose rate rather than activity is required.
		β	Extrapolation ionization chamber.	do	
II *In vivo* measurement	Quantitative	γ	Fixed geometry scintillation crystals (inorganic).	At 20–30 cm 1 μc I–131 up.	Large crystal necessary to achieve lower limit.
			Geiger-Müller counter	8 μc I–131 up	Bismuth cathode tube for I–131.
	Distribution	γ	Scintiscanner (inorganic crystal and mechanical scan).	5 μc I–131 up	Large crystal and wide-angle collimator necessary to achieve lower limit.
	Quantitative and distribution	β	End-window or needle Geiger-Müller system.	0.0005 μc P–32 up	

Preferred methods of measurement for clinical and biological purposes—Continued

Class		Purpose	Radiation	Type	Approximate sensitivity	Remarks
III	Post-administration measurement	Excreta samples (total volume)	γ and *bremsstrahlung*.	Scintillation crystal (inorganic)	0.01 μc I–131 up	Efficiency for I–131 and Co–60 very similar.
				Ring of large Geiger-Müller counters.	0.1 μc I–131 up	
		Blood and other small samples	γ and *bremsstrahlung*.	Well scintillation counter	0.00005 μc I–131	Efficiency for I–131 and Co–60 very similar.
			β	Cylindrical jacketed Geiger-Müller counter.	0.00005 μc P–32	Sensitivity depends on beta energy.
			low energy β	Gas-flow Geiger-Müller counter	0.0001 μc C–14	Sensitivity depends primarily on sample preparation.
		Chromatographic and autoradiographic samples, etc.	β	End-window Geiger-Müller or gas-flow Geiger-Müller system.	0.0002 μc/cm^2 C–14	Sensitivity varies according to radionuclide studied.
IV	Other	Routine laboratory monitoring	β γ	Geiger-Müller counter	0.0001 μc P–32 up	
				do	0.01 μc I–131 up	
		Disposal	γ and *bremsstrahlung*.	Simple fixed geometry Geiger-Müller or scintillation system.	0.1 μc to 1 mc	
				Calibrated ionization chamber	1 mc up	

Appendix C

Measurements necessary in diagnostic techniques

Technique	Radionuclide	Approximate amount used μc[1]	Bulk calibration	Checking of aliquot for administration	*In vivo* quantitative	*In vivo* distribution	Excreta samples	Blood or other	Laboratory monitoring	Disposal
Thyroid studies:										
Uptake, excretion	I-131	1–25	x	x	x		x		x	x
PBI	I-131	50–100	x	x				x	x	x
I-131 distribution	I-131	25–250	x	x		x			x	x
Uptake in metastases	I-131	50–500	x	x	x	x			x	x
Cardiac output	I-131 or other	50–100	x	x	x			x	x	x
Liver localization	I-131 Au-198	200–1,000	x	x		x			x	x
Liver function	I-131	5–200	x	x	x				x	x
Gall bladder	I-131	25–50	x	x		x			x	x
Kidney function	I-131	25–50	x	x		x			x	x
Pancreatic insufficiency or fat metabolism	I-131	25–50	x	x			x	x	x	x
Brain tumor	I-131 As-74	200–500	x	x		x			x	x
Blood volume	I-131	10–25	x	x				x	x	x
	Cr-51	20–100	x	x				x	x	x
Malignant uptake	P-32, Y-90	100–750	x			x			x	x
Iron turnover	Fe-59	10	x	x				x	x	x
Red cell survival	Cr-51	20–100	x	x				x	x	x
Schilling test	Co-60	0.25–0.5		x			x		x	x
Circulation, vascularity	Na-24	20–100	x	x		(x)		x	x	x
	I-131	50–200	x	x		(x)		x	x	x

[1] Minimum amount possible should be used. This amount is usually determined by the sensitivity of the equipment used.

Appendix D

Measurements necessary in therapeutic techniques

Technique	Radionuclide	Approximate amount used mc [1]	Bulk calibration	Checking of aliquot for administration	*In vivo* quantitative	*In vivo* distribution	Excreta samples	Blood or other	Laboratory monitoring	Disposal	Measurement of dose rate	
											γ	β
I-131 therapy:												
Hyperthyroid	I-131	1–10	x	(x)	x	x	x	x	x	x		
Cardiac	I-131	10–25	x	(x)	x	x	x	x	x	x		
Cancer	I-131	25–250	x	(x)	x	x	x	x	x	x		
Blood dyscrasia (i.v.)	P-32	1–6	x	x			x		x	x		
Late bone metastases (i.v.)	P-32	3–15	x	x			x		x	x		
Intracavitary, peritoneal and pleural.	Au-198	50–200	x	x		x	x		x	x		
	$CrP^{32}O_4$	5–15	x	x			x		x	x		
	Y-90											
Interstitial colloid	Au-198	20–100	x	x		x	x		x	x		
Interstitial and superficial metallic sources.	Au-198	5–150 not permanent.	x	x		(x)			x	x	x	
	Ir-192											
	Ta-182											
	Co-60											
	Ra-226											
Intracavitary bladder	Br-82	100–300	x	x		(x)	x		x	x	x	
	Au-198											
Beta applicators	P-32	2–25							x			x
	Sr-90/Y-90	5–100							x			x
	Ra D+E											

[1] Amounts used vary according to the dose it is desired to give, and are not determined by the sensitivity of the measuring system.

14. General References

Beierwaltes, W. H., Johnson, P. C., and Solair, A. J. (1957). Clinical use of radioisotopes (W. B. Saunders Co., Philadelphia).

Blahd, W. H., Bauer, F. K., and Cassen, B. (1958). The practice of nuclear medicine (C. C Thomas, Springfield, Ill.).

Blatz, H. Editor-in-Chief (1959). Radiation hygiene handbook (McGraw-Hill Book Co., Inc., New York, N.Y.).

Blanchard, R. L., Kahn, B., and Birkhoff, R. D., (1960). The preparation of thin, uniform, radioactive sources by surface adsorption and electrodeposition, Health Physics **2**, 246.

Boyd, G. A. (1955). Autoradiography in biology and medicine (Academic Press, Inc., New York, N.Y.).

Comar, C. L. (1955). Radioisotopes in biology and agriculture (McGraw-Hill Book Co., Inc., New York, N.Y.).

Evans, R. D. (1955). The atomic nucleus (McGraw-Hill Book Co., Inc., New York, N.Y.).

Friedlander, G., and Kennedy, J. W. (1955). Nuclear and radiochemistry (J. Wiley and Sons, Inc., New York).

Hine, G. J., and Brownell, G. L., Editors (1956). Radiation dosimetry (Academic Press, Inc., New York, N.Y.).

Kamen, M. D. (1957). Isotopic tracers in biology, 3d ed. (Academic Press, Inc., New York, N.Y.).

Mann, W. B., and Seliger, H. H. (1958a). Preparation, maintenance, and application of standards of radioactivity, NBS Circular 594.

Price, W. J. (1958). Nuclear radiation detection (McGraw-Hill Book Co., Inc., New York, N.Y.).

Quimby, E. H. (1960). Safe handling of radioactive isotopes in medical practice (The Macmillan Co., New York, N.Y.).

Quimby, E. H., Feitelberg, S., and Silver, S. (1958). Radioactive isotopes in clinical practice (Lea & Febiger, Philadelphia, Pa.).

Siegbahn, Kai, (Editor) (1955). Beta- and gamma-ray spectroscopy (North-Holland Publishing Co., Amsterdam).

Slack, L., and Way, K. (1959). Radiations from radioactive atoms in frequent use (U.S. Government Printing Office, Washington 25, D.C.).

Veall, N., and Vetter, H. (1958). Radioisotopes techniques in clinical research and diagnosis (Butterworth & Co., London).

Federal Register, vol. **22**, No. 19, Washington, January 29, 1957, Title 10—Atomic Energy, ch. I—Atomic Energy Commission, Pt. 20—Standards for protection against radiation.

Metrology of Radionuclides, Proceedings of a Symposium organized by the International Atomic Energy Agency (Vienna 1960).

ICRU-NBS Handbook 78, Report of the International Commission on Radiological Units and Measurements (ICRU) 1959 (1961).

The Isotope Index (Scientific Equipment Co., Indianapolis, Ind.).

National Academy of Sciences-National Research Council Publication 467, Multichannel pulse height analyzers.

National Academy of Sciences-National Research Council Publication 573, Measurements and standards of radioactivity.

National Committee on Radiation Protection and Measurements—National Bureau of Standards Handbooks (U.S. Government Printing Office, Washington 25, D.C.):

No. 42.—Safe handling of radioactive isotopes (1949).

No. 48.—Control and removal of radioactive contamination in laboratories (1951).

No. 49.—Recommendations for waste disposal of phosphorus-32 and iodine-131 for medical users (1951).

No. 53.—Recommendations for the disposal of carbon-14 wastes (1953).
No. 58.—Radioactive-waste disposal in the ocean (1954).
No. 64.—Design of free-air ionization chambers (1957).
No. 65.—Safe handling of bodies containing radioactive isotopes (1958).
No. 69.—Maximum permissible amounts of radioisotopes in the human body and maximum permissible concentrations of air and water (1959).
No. 79.—Stopping powers for use with cavity chambers (1961).
No. —.—Handling of radioactive nuclides and fission products (Revision of NCRP-NBS Handbook 42 in preparation).

Nuclear instrumentation, Handbuch der Physik **45** (Springer, Berlin-Göttingen-Heidelberg).

Nucleonic instrumentation, A Special Report, Nucleonics **17**, 6, 63.

Radioisotopes in scientific research, Proceedings of the First (UNESCO) Scientific Conference, vol. **I-IV** (Pergamon Press, London and New York).

Report on international conference on autoradiography 1958, Laboratory Investigation **8**, No. 1 (Jan.–Feb. 1959).

Safe handling of radioisotopes, International Atomic Energy Agency Safety Series, No. 1 (Vienna, 1958).

15. References

Allen, H. C., Jr., Libby, R. L., and Cassen, B., (1951) The scintillation counter in clinical studies of human thyroid physiology using I-131, J. Clin. Endocrinol, **11,** 492.

Allen, H. C., Jr., and Risser, J. R. (1955). Simplified apparatus for brain tumor surveys, Nucleonics, **13,** No. 1, 28.

Allen, R. A. (1957). The standardization of electron capture isotopes, Int. J. Appl. Radiation and Isotopes, **1,** 289.

Alper, T., and du Preez, L. (1949). Use of bremsstrahlung in making rapid assays of millicurie amounts of P-32, Nature, **164,** 1001.

Anderson, E. C., Libby, W. F., Weinhouse, S., Reid, A. F., Kirshenbaum, A. D., and Grosse, A. V., (1947). Natural radiocarbon from cosmic radiation, Phys. Rev. **72,** 931.

Anderson, E. C., Schuch, R. L., Perrings, J. D., and Langham, W. H. (1956). The Los Alamos human counter, Nucleonics **14,** No. 1, 26.

Anger, H. O. (1952). Use of gamma-ray pinhole camera for *in vivo* Studies, Nature **170,** 200.

Anger, H. O. (1953). A multiple scintillation counter *in vivo* scanner, Amer. J. Roentgenol. **70,** 605.

Anger, H. O. (1958). Scintillation camera, Rev. Sci. Instr. **29,** 27.

Armstrong, W. D., Singer, L., Zbarsky, S. H., and Dunshee, B. (1950). Errors of combustion of compounds for C^{14} analysis, Science **112,** 531.

Attix, F. H., and Ritz, V. H. (1957). A determination of the gamma-ray emission of radium, J. Research NBS **59,** 293, RP2801.

Audric, B. N., and Long, J. V. P. (1952). Measurement of low-energy β-emitters by liquid scintillation counting, Research **5,** 46.

Audric, B. N., and Long, J. V. P. (1953). The background and ^{14}C detection efficiency of a liquid scintillation counter, J. Sci. Instr. **30,** 467.

Barnothy, J., and Farro M. (1951). Coincidence methods of measuring disintegration rates of radioactive sources, Rev. Sci. Instr. **22,** 415.

Barron, J. N., Veall, N., and Arnott, D. G. (1951). Measurement of the local clearance of radioactive sodium in tubed skin pedicles, Brit. J. Plast. Surg. **4,** 16.

Basson, J. K., and Steyn, J. (1954). Absolute alpha standardization with liquid scintillators, Proc. of Phys. Soc., (**A**) **67,** 297.
Bauer, F. K., Goodwin, W. E., Libby, R. L., and Cassen, B., (1952). Visual delineation of thyroid glands *in vivo,* J. Lab. Clin. Med. **39,** 153.
Bay, Z. (1956). Techniques and theory of fast coincidence experiments, IRE Trans. on Nuclear Science, **NS–3,** 12.
Bay, Z., Mann, W. B., Seliger, H. H., and Wyckoff, H. O. (1957). Absolute measurement of W_{air} for sulfur-35 beta rays, Radiation Research, **7,** 558.
Bayly, J. G. (1950). A calorimetric measurement of the disintegration rate of a P^{32} source, Can. J. Research **A28,** 520.
Beierwaltes, W. H., Johnson, P. C., and Solair, A. J. (1957). Clinical use of radioisotopes (W. B. Saunders Co., Philadelphia, Pa.)
Belcher, E. H. (1953). Scintillation counters using liquid luminescent media for absolute standardization and radioactive assay, J. Sci. Instr. **30,** 286.
Bell, C. G., and Hayes, F. N., Editors (1958). Liquid scintillation counting, proc. conf. held at Northwestern University (Pergamon Press, London and New York).
Bender, M. A. (1957). Photoscanning detection of radioactive tracers *in vivo,* Science **125,** 443.
Berman, M., Schoenfeld, R. (1956). Invariance in experimental data on linear kinetics and the formation of models, J. Appl. Phys. **27,** 1361.
Bernstein, W., and Ballentine, R., (1950). Gas phase counting of low energy beta-emitters (spherical proportional gas counter is also described in this paper), Rev. Sci. Instr. **21,** 158.
Birks, J. B. (1953). Scintillation counters (McGraw-Hill, Inc., New York, N.Y.).
Block, R. J., Durrum, E. L., and Zweig, G., (1958). Paper chromatography and paper electrophoresis (Academic Press, Inc., New York, N.Y.).
Blumfield, G. W., Jones, T. C., MacGregor, A. G., Miller, H., and Wayne, E. J. (1951). Treatment of thyrotoxicosis with radioactive iodine, Brit. Med. J. **2,** 373.
Bortner, T. E. (1951). An extrapolation chamber: construction and use, Nucleonics, **9,** No. 3, 40.
Bortner, T. E., and Hurst, G. S. (1954). Ionization of pure gases and mixtures of gases by 5-Mev Alpha particles, Phys. Rev. **93,** 1236.
Bourne, G. H. (1952). Autoradiography, Biol. Rev. Cambridge Phil. Soc. **27,** 108.
Boyd, G. A. (1955). Autoradiography in biology and medicine (Academic Press, Inc., New York, N. Y.).
Brown, Daniel A. (1957). Tritium separation factor in the calcium-water reaction, U.S. Atomic Energy Commission Report DP–217.
Brown, S. C., and Miller, W. W., (1947). Carbon dioxide filled Geiger-Müller counters Rev. Sci. Instr. **18,** 496.
Brownell, G. L. (1958). Theory of radioisotope scanning, Int. J. Appl. Rad. Isotopes, **3,** 181.
Brownell, G. L., and Lockhart, H. S. (1952). Co_2 ion chamber techniques for radiocarbon measurement, Nucleonics **10,** No. 2, 26.
Brownell, G. L., and Stanbury, J. B. (1953). Instrumentation for thyroid measurement, J. Clin. Endocrinol. **13,** 210.
Brownell, G. L., and Sweet, W. H. (1953). Localization of brain tumors with positron emitters, Nucleonics **11,** No. 11, 40.
Broyles, C. D., Thomas, D. A., and Haynes, S. (1953). Measurement and interpretation of the K Auger intensities of Sn^{113}, Cs^{137}, and Au^{198}, Phys Rev. **89,** 915.

Brucer, H. M. (1955). Thyroid radioiodine uptake calibration, Geneva Conference on the Peaceful Uses of Atomic Energy, United Nations.
Brucer, H. M. (1958). Radioisotope Scanning, Oak Ridge Institute of Nuclear Studies Report, ORINS–20.
Brucer, H. M., Oddie, T. H., and Eldridge, J. S. (1956). Thyroid uptake calibration I mock iodine, a radioactive iodine gamma-ray standard, Oak Ridge Institute of Nuclear Studies, ORINS–14, July 25, 1956.
Brysk, H., and Rose, M. E., (1958). Theoretical results on orbital electron capture, Rev. Mod. Phys. **30,** 1169.
Burch, P. R. J., and Spiers, F. W. (1953). Measurement of γ-radiation from the human body, Nature **172,** 519.
Calvin, M., Heidelberger, C., Reid, J. C., Tolbert, B. M., and Yankwich, P. F. (1949). Isotopic carbon (John Wiley & Sons, Inc., New York, N. Y.).
Campion, P. J. (1959). The standardization of radioisotopes by the beta-gamma coincidence method using high efficiency detectors, Int. J. Appl. Rad. Isotopes **4,** 232.
Campion, P. J., and Merritt, W. F. (1957). The standardization of electron capturing nuclides: A preliminary study, Atomic Energy of Canada Limited, Report CRP 745.
Campion, P. J., Taylor, J. G. V., and Merritt, J. S. (1960). The efficiency tracing technique for elimination of self-absorption errors in 4π β-counting, Int. J. Appl. Rad. and Isotopes **8,** 8.
Carswell, D. J., and Milsted, J. (1957). A new method for the preparation of thin films of radioactive material, J. Nuclear Energy I **4,** 51.
Cassen, B., Curtis, L., Reed, C., and Libby, R. (1951). Instrumentation for I-131 Use in Medical Studies, Nucleonics **9,** No. 2, 46.
Cassidy, H. G. (1951). Adsorption and Chromatography (Interscience Publishers, Inc., New York, N.Y.).
Catz, B., and Starr, P. (1956). Carcinoma of the thyroid with metastases to the lungs; condition shown by scintigram in absence of definite X-ray findings, J. Amer. Med. Assoc. **160,** 1046.
Chamberlain, R. H. (1953). The place of physics in clinical radiology, Radiology **60,** 331.
Christman, D. R., Day, N. E., Hansell, P. R., and Anderson, R. C. (1955). Improvements in isotopic C assay and chemical analysis of organic compounds by dry combustion, Analytical Chemistry **27,** 1935.
Christman, D. R., and Wolf, A. P. (1955). Inherent errors and lower limit of activity detection in gas-phase proportional counting of carbon-14, Analytical Chemistry **27,** 1939.
Christman, D. R., Stuber, J. E., and Bothner-by, A. A. (1956). Dry combustion and volumetric determination of isotopic C and H in organic compounds, Analytical Chemistry **28,** 1345.
Churchill, R. V. (1944). Modern operational mathematics in engineering (McGraw-Hill Book Co., Inc., New York, N.Y.).
Clarke, R. K. (1950). Absolute determination of the emission rate of beta rays, Columbia University Radiological Research Laboratory Report NYO–1506.
Collins, V. C. (1956). Exhibit, american roentgen ray society, Washington, D. C.
Collinson, A. J. L., Demetsopoullos, I. C., Dennis, J. A., and Zarzycki, J. M. (1960). Self-quenching geiger counters containing mixtures of permanent gases. Nature **185,** 369.

Comar, C. L. (1948). Radioisotopes in nutritional trace element studies I, Nucleonics **3,** No. 3, 32.
Comar, C. L. (1955). Radioisotopes in biology and agriculture—principles and practice (McGraw-Hill Book Co., Inc., New York, N.Y.).
Condon, E. V., and Odishaw, H. (1958). Handbook of Physics (McGraw-Hill Book Co., Inc., New York, N.Y.).
Concannon, J. P., and Bulluis, F. (1957). Studies with a modified collimator for use with scintillation counter for total body scanning, Amer. J. Roentgenol. **78,** 855.
Conway, H., Roswit, B., Stark, R. B., and Yalow, Rosalyn (1951). Radioactive sodium clearance as a test of circulatory efficiency of tubed pedicles and flaps, Proc. Soc. exp. Biol. **77,** 348.
Corbett, B. D., and Honour, A. J. (1951). Design of directional counters for clinical use, Nucleonics **9,** No. 5, 43.
Corbett, B. D., Cunningham, R. M., Halnan, K. E., and Pochin, E. E. (1956). A profile counter and its calibration, Phys. Med. Biol. **1,** 37.
Cunningham, R. M., Hilton, G. H., and Pochin, E. E. (1955). Radioiodine uptake in thyroid carcinomata, Brit. J. Radiol. **28,** 252.
Curran, S. C. (1950). Counting and spectrometry with proportional tubes, Atomics, **1,** 221.
Curran, S. C., Angus, J., and Cockroft, A. L., 1949. Investigations of soft radiations by proportional counters, Phil. Mag. **40,**, 36.
Curtis, L., and Cassen, B. (1952). Speeding up and improving contrast of thyroid scintigrams, Nucleonics **10,** No. 9, 58.
Damon, P. E., and Winters, P. N. (1954). Resolution losses in counters and trigger circuits, Nucleonics **12,** No. 12, 36.
Davidson, J. D., and Feigelson, P. (1957). Practical aspects of internal-sample liquid scintillation counting, Int. J. Appl. Rad. and Isotopes **2,** 1.
De Benedetti, S., and Findley, W., (1958). The coincidence method, Handbuch der Physik, **45,** 222.
Desty, D. H., and Harbourn, C. L. A. (1957). Vapour phase chromatography (Butterworth's Scientific Publications, London).
Dubridge, L. A., and Brown, H. (1933). An improved d.c. amplifying circuit, Rev. Sci. Instr. **4,** 532.
Dunworth, J. V. (1940). The application of the method of coincidence counting to experiments in nuclear physics, Rev. Sci. Instr. **11,** 167.
Elmore, W. C. (1950). Statistics of counting, Nucleonics, **6,** No. 1, 26.
Elmore, W. C., and Sands, M. (1949). Electronics (McGraw-Hill Book Co., Inc., New York, N.Y.).
Engelkemeir, A. G., Hamill, W. H., Inghram, M. C., and Libby, W. F., (1949). The half-life of radiocarbon (C^{14}), Phys. Rev. **75,** 1825.
Engelkemeir, A. G., and Libby, W. F., (1950). End and wall corrections for absolute beta-counting in gas counters, Rev. Sci. Instr. **21,** 550.
Evans, R. D. (1955). The atomic nucleus (McGraw-Hill Book Co., Inc., New York, N.Y.).
Evans, R. D., and Evans, R. O. (1948). Studies of self-absorption in gamma-ray sources, Rev. Mod. Phys. **20,** 305.
Failla, G. (1937). The measurement of tissue dose, Radiology, **29,** 202.
Failla, G., Rossi, H. H., Clarke, R. K., and Bailey, N. (1947). The measurement of tissue dose of ionizing radiation I. Beta ray emitting isotopes uniformly distributed in a homogeneous tissue, U.S. Atomic Energy Commission Report AECD–2142.
Failla, G., and Gross, W. (1952). Annual Report on Research Project AEC Declassified Document NYO–4008, 57.

Fairstein, E. (1956). Non-blocking double-line linear pulse amplifier Rev. Sci. Instr. **27,** 475.
Feingold, Q. M., and Frankel, S. (1955). Geometrical corrections in angular correlation instruments, Phys. Rev. **97,** 1025.
Feitelberg, S. (1949). Standardization of radioactive iodine, Science **109,** 456.
Feitelberg, S., Kaunitz, P. E., Wasserman, L. R., and Yohalem, S. B. (1948). The use of radioactive iodine in the diagnosis of thyroid disease, Amer. J. Med. Sci. **216,** 129.
Fisher, R. A. (1950). Statistical methods for research workers (Hafner Publishing Co., New York, N.Y.).
Fitzgerald, P. J. (1952). Radioautography in cancer, Cancer **5,** 165.
Fitzgerald, P. J., Simmel, Eva, Weinstein, J., and Martin, Cynthia (1953). Radioautography: theory, technic and applications, Lab. Invest. **2,** 181.
Francis, J. E., Ball, R. P., and Harris, C. C. (1955). Medical scintillation spectrometer, Nucleonics **13,** No. 11, 82.
Frantz, V. K., Ball, R. P., Keston, A. S., and Palmer, W. W. (1944.) Thyroid carcinoma with metastases: studied with radioactive iodine Ann. Surg. **119,** 668.
Friedell, H. L., MacIntyre, W. J., and Rejali, A. M. (1957). Method for visualization of configuration and structure of liver. Part A, preliminary clinical investigations, Am. J. Roentgenol. **77,** 455.
Friedell, M. T., Schaffner, F., Pickett, W. J., and Hummon, I. F. (1949). Radioactive isotopes in the study of peripheral vascular disease. I, Arch. Intern. Med. 83, 608; II Arch. Intern. Med. **83,** 620.
Friedlander, G., and Kennedy, J. W. (1955). Nuclear and radiochemistry (John Wiley & Sons, Inc., New York).
Friedman, H. (1949). Geiger counter tubes, Proc. IRE **37,** 791.
Gandy, A., 1961. Mesure absolue de l'activité des radionuclides par la méthode des coincidences béta-gamma a l' aide de détecteurs de grande efficacité: Étude des coincidences instrumentales. In publication.
Garfinkel, S. B. (1959). Semiautomatic Townsend balance system, Rev. Sci. Instr. **30.**
Garrett, C. (1958). Modification of the basis for roentgen calibrations between 0.5 and 3 Mev, Can. J. Phys. **36,** 149.
Glasscock, R. F. (1954). Isotopic gas analysis for biochemists (Academic Press, Inc., New York, N.Y.).
Glasscock, R. F. (1955a). Gas counting techniques in biochemistry. Combustion of labelled compounds and gas counting of C^{14}, Atomics **6,** 329.
Glasscock, R. F. (1955b). Gas counting techniques in biochemistry II. Determination of H^3 and applications of gas counting to biochemical research, Atomics **6,** 329.
Goldberg, I. J. L., and Fitzsimons, E. A. (1958). The thyroidal accumulation of radioiodine as a clinical test for hyperthyroidism, Brit. J. Radiol. **31,** 428.
Goolden, A. W. G. (1958). A comparison of radioiodine tests in the diagnosis of hyperthyroidism, Brit. J. Radiol. **31,** 433.
Gray, L. H. (1944). The ionization method of measuring neutron energy, Proc. Camb. Phil. Soc. **40,** 73.
Gray, L. H. (1949). The experimental determination by ionization methods of the rate of emission of beta- and gamma-ray energy by radioactive substances, Brit. J. Radiol. **22,** 677.
Gross, J. R. B., Bogoroch, R., Nadler, N. J., and Leblond, C. P. (1951). The theory and methods of the radioautographic localization of radioelements in tissues, Amer. J. Roentgenol. **65,** 420.

Gross, W., and Failla, G. (1950). A new method of radioactivity measurement, Phys. Rev. **79,** 209.
Gross, W., Wingate, C., and Failla, G. (1957). Determination of disintegration rate for gamma-emitting isotopes, Radiology **69,** 699.
Gross, W., Wingate, C., and Failla, G. (1957). The average energy lost by S^{35} beta rays per ion pair produced in air, Radiation Research **7,** 570.
Grummitt, W. E., Brown, R. M., Cruikshank, A. J., and Fowler, I. L. (1956). Recent developments in low-background Geiger-Müller counters, Can. J. Chem. **34,** 206.
Hahn, O. (1936). Applied radiochemistry (Cornell University Press, New York, N.Y.).
Halliday, D. (1955). Introductory Nuclear Physics, 2d ed. (John Wiley & Sons, Inc., New York, N.Y.).
Harnwell, G. P., and Livingood, J. J. (1933). Experimental atomic physics, (McGraw-Hill Book Co., Inc., New York, N.Y.).
Harris, C. C., Hamblen, D. P., and Francis, J. E. (1959). Basic principles of scintillation counting for medical investigation, Oak Ridge National Laboratory Report No. 2808.
Harrison, F. B., Slow component decay of fluors, Nucleonics **12,** No. 3, 24.
Hawkings, R. C., Hunter, R. F., and Mann, W. B., (1949). On the efficiency of gas counters filled with carbon dioxide and carbon disulfide, Can. J. Research [B] **27,** 555.
Hawkings, R. C., Hunter, R. F., Mann, W. B., and Stevens, W. H. (1949). The half-life of C^{14}, Can. J. Research **27,** 545.
Hawkings, R. C., and Merritt, W. F. (1954). Some preliminary results on the absolute beta counting of tritium, Atomic Energy of Canada Limited, Report 94.
Hawkings, R. C., Merritt, W. F., and Craven, J H. (1952). The maintenance of radioactive standards with 4π proportional counter, Proceedings of Symposium, National Physical Laboratory, May 1951 (H. M. Stationery Office, London).
Haybittle, J. L. (1955). Ionization chambers for the dosimetry of beta-ray applicators, Brit. J. Radiol. **28,** 320.
Hayward, R. W., Hoppes, D. D., and Mann, W. B. (1955). Branching ratio in the decay of polonium-210, J. Research NBS **54,** 47, RP2564.
Heath, R. L. (1957). Scintillation spectrometry gamma ray spectrum catalogue, U.S. Atomic Energy Commission Report IDO 16408.
Heintze, J., and Fischbech, H. (1957). Absolute beta counting in samples of saturation thickness, Z. Phys. **147.**
Heller, D. A. (1951). The radioautographic technique, Advances in Biol. and Med. Phys. **2,** 133.
Henry, W. H. (1957). Private communication.
Herz, R. H. (1951). Photographic fundamentals of autoradiography, Nucleonics **9,** No. 3, 324.
Hine, G. J., and Brownell, G. L., Editors (1956). Radiation dosimetry (Academic Press, Inc., New York, N.Y.).
Hönigschmid, O. (1945). Geschichte und Herstellung der primären Radium-Standards, Anz. Akad. Wiss., Wien, 82, 30.
Horowitz, N. H., and Lofstrom, J. E. (1955). Photographic recording methods for scintillation scanning, Nucleonics **13,** No. 7, 56.
Howard, N., McAlister, J. M., and McEvedy, M. B. (1958). Factors affecting the choice of a routine radioactive iodine test for thyroid activity, Brit. J. Radiol. **31,** 437.
Hudswell, F., (1949). The preparation of films and coatings, Atomic Energy Research Establishment Report AERE CIR 392 (October 1949).

Huff, R. L., and Judd, O. A. (1956). Kinetics of iron metabolism, Advances in Biological and Medical Physics **IV** (Academic Press, Inc., New York, N.Y.).
Hughes, D. J. (1953). Pile neutron research (Addison-Wesley Publishing Co., Cambridge, Mass.).
Hughes, D. J., and Schwartz, R. B. (1958). Neutron cross-sections, Brookhaven National Laboratory Report No. 325.
Ittner, W. B., III, and Ter-Pogossian, M. (1951). Scintillation detector for the localization of radioactive concentration *in vivo*, Rev. Sci. Instr. **22,** 638.
Jacobs, M. E., Orvis, A. L., and Borrman, B. B. (1954). Electric recorder for gamma-graph, Nucleonics **12,** No. 1, 60.
Jaeger, J. C. (1956). An introduction to the Laplace transformation, Methuen & Co., Ltd., London.
Jansson, L., Larsson, L. G., and Raynholt, J. (1957). A scanning apparatus for the localization of gamma emitting isotopes *in vivo*, Acta Radiol. **47,** 217.
Jesse, W. P., and Sadauskis, J. (1953). Alpha-particle ionization in pure gases and the average energy to make an ion pair, Phys. Rev. **90,** 1120.
Jesse, W. P., and Sadauskis, J. (1955). Ionization in pure gases and the average energy to make an ion pair for alpha and beta particles, Phys. Rev. **99,** 1668.
Jones, W. M., (1949). A determination of the half-life of carbon 14, Phys. Rev. **76,** 885.
Jones, W. M., (1951) (36). The half-life of tritium by absolute counting, Phys. Rev. **83,** 537.
Kamen, M. D. (1957). Isotopic tracers in biology, 3d ed. (Academic Press, Inc., New York, N.Y.).
Keene, J. P. (1950). An absolute method for measuring the activity of radioactive isotopes, Nature **166,** 601.
Kelly, G. G. (1956). The A–8 linear amplifier, Oak Ridge National Laboratory Report ORNL 2204.
Kendall, M. G., and Buckland, W. R. (1957). A dictionary of statistical terms; (International Statistical Institute, Paris.).
Kety, S. S. (1952). Measurement of regional circulation by local clearance of radioactive sodium, J. Am. Heart **43,** 67.
Kramer, S., Concannon, J. P., Evans, H. D., and Clark, G. M. (1955). Report on diagnostic and therapeutic use of radioiodine, Brit. J. Radiol. **28,** 307.
Krohmer, J. S. (1951). Physical measurements in various beta-ray applicators, J. Amer. Roentgenol. **66,** 791.
Kuhl, D. E., Chamberlain, R. H., Hale, J., and Gorson, R. O. (1956). A high contrast photographic recorder for scintillation counter scanning, Radiology **66,** 730.
Kusner, D. B. (1956). Private communication.
Laurence, J. H., and Tobias, C. A., Editors, (1953). Advances in biological and medical physics, **3** (Academic Press, Inc., New York).
Leblond, C. P., and Gross, J. (1951). Autoradiography as a tool in medical research, ch. 12 in A Manual of Artificial Radioisotope Therapy, edited by P. F. Hahn (Academic Press, Inc., New York).
Lederer, E., and Lederer, M. (1957). Chromatography, 2d ed. (Elsevier's Wetenschappelijke Uitegeveri, Amsterdam).
Libby, W. F. (1957). Isotopes in chemistry teaching, J. Chem. Educ. **34,** 578.
Liebson, S. H., and Friedman, H. (1948). Self-quenching halogen-filled cavities, Rev. Sci. Instr., **19,** 303.
Loevinger, R. (1953). Extrapolation chamber for the measurement of beta sources, Rev. Sci. Instr. **24,** 907.

Loevinger, R. (1957). Average energy of allowed beta-particle spectrum. Physics in Medicine and Biology **1,** 330.
Loevinger, R., and Berman, M. (1951). Efficiency criteria in radioactivity counting, Nucleonics **9,** No. 1, 26.
Loevinger, R., and Feitelberg, S. (1955). Using Brensstrahlung detection by a scintillator for simplified beta counting; Nucleonics **13,** No. 4, 42.
Lyon, W. S., and Reynolds, S. A. (1956). Alpha-gamma coincidence counting for flow-counter calibration, Nucleonics **14,** No. 12, 44.
Lyon, W. S., and Reynolds, S. A. (1957). The assay of electron capture nuclides with a proportional counter spectrometer, Int. J. Appl. Rad. Isotopes **2,** 80.
MacIntyre, W. J., Storaasli, J. P., Krieger, H., Pritchard, W., and Friedell, H., (1952). I^{131} Labelled serum albumin; its use in the study of cardiac output and peripheral vascular flow, Radiology **59,** 849.
MacIntyre, W. J., and Houser, T. S. (1957). Method for visualization of configuration and structure of liver. Part B., Counting rate cut-off circuit for increased contrast in automatic scanning, Am. J. Roentgenol. **77,** 471.
Makower, W. (1909). On the number and the absorption by matter of the β particles emitted by radium, Phil. Mag. (6) **17,** 171.
Mann, W. B. (1954a). Use of Callendar's "radio-balance" for the measurement of the energy emission from radioactive sources; J. Research NBS **52,** 177, RP2486.
Mann, W. B. (1954b). A radiation balance for the microcalorimetric comparison of four national radium standards, J. Research NBS **53,** 277, RP2545.
Mann, W. B. (1958). Counting of low energy radiation for the standardization of low-energy beta emitters and electron capturers, Proc. Symposium on Measurements and Standards of Radioactivity, National Academy of Sciences, National Research Council Nuclear-Science Series No. 24, publication 513.
Mann, W. B., and Parkinson, G. B. (1949). A Geiger-Müller counting unit and external quenching equipment for the estimation of C^{14} in carbon dioxide, Rev. Sci. Instr. **20,** 41.
Mann, W. B., and Seliger, H. H. (1953). Refinements in radioactive standardization by 4π Counting, J. Research NBS **50,** 197, RP2409.
Mann, W. B., and Seliger, H. H. (1958a). Preparation, maintenance, and application of standards of radioactivity, NBS Circ. 594.
Mann, W. B., and Seliger, H. H. (1958b). Radioactivity standardization in the United States, Proc. Second United Nations Inter. Conf. on the Peaceful Uses of Atomic Energy, **21,** 90.
Mann, W. B., Seliger, H. H., Marlow, W. F., and Medlock, R. W. (1960). A recalibration of NBS carbon-14 standards by Geiger-Müller and proportional gas counting, Rev. Sci. Instr. **31,** 690.
Mann, W. B., Stockmann, L. L., Youden, W. J., Schwebel, A., Mullen, P. A., and Garfinkel, S. B. (1959). The preparation of new solution standards of radium, J. Research NBS **62,** 27, RP2924.
Manov, G., and Curtiss, L. F. (1951). The half-life of carbon-14, J. Research NBS **46,** 328, RP2203.
Marinelli, L. D., Miller, C. E., Gustafson, P. F., and Roland, R. E. (1955). Determination of γ-ray emitting elements, Am. J. Roentgenol. **73,** 661.
Marlow, W. F., and Medlock, R. W. (1960). Preparation and standardization of a carbon-14 beta-ray standard: benzoic-acid-7-C^{14} in toluene, J. Research NBS 64**A,** 143.

Mayneord, W. V., Turner, R. C., Newberry, S. P., and Hodt, H. J. (1951). A method of making visible the distribution of activity in a source of ionizing radiation, Nature **168,** 762.
Mayneord, W. V., and Newberry, S. P. (1952). Automatic method of studying distribution of activity in source of ionizing radiation, Brit. J. Radiol. **25,** 589.
Mayneord, W. V. (1953). Scintillation counting and its medical applications, Brit. J. Appl. Phys. **4,** 353.
Mayneord, W. V. (1954). Radiological research, Brit. J. Radiol. **27,** 309.
Mayneord, W. V., Evans, H. D., and Newberry, S. P. (1955). An instrument for the formation of visual images of ionizing radiations, J. Sci. Instr. **32,** 45.
McNish, A. G. (1958). Classification and nomenclature for standards of measurement, IRE Trans. on Instrumentation, I **7,** 371.
McNish, A. G. (1960). Nomenclature for standards of radioactivity, int. J. Applied Radiation and Isotope, 145.
Merritt, J. S., Taylor, J. G. V., and Campion, P. J., (1959). Self absorption in sources prepared for 4π beta counting, Can. J. Chem. **37,** 1109.
Merritt, W. F., and Hawkings, R. C. (1960). The absolute assay of S^{35} by internal gas counting, Anal. Chem. (Submitted for publication).
Merritt, J. S., Taylor, J. G. V., Merritt, W. F., and Campion, P. J. (1960). The absolute counting of sulfur-35, Anal. Chem. **32,** 310.
Merritt, W. F. (1958). System for counting tritium as water vapor, Anal. Chem. **30,** 1745.
Meyer-Schützmeister, L., and Vincent, D. H. (1952). Absoluteichungen energiearmer β Strahler mit dem 4π-Zählrohr, Z. für Physik **134,** 9.
Middleton, G., and Stuckey, R. E. (1953). The preparation of biological material for the determination of trace metals, I. A critical review of existing procedures, Analyst **78,** 532.
Miller, E. R., and Scofield, N. E. (1955). Studies with radioiodine. IV: Collimating cones for crystal counters, Radiol. **65,** 96.
Miller, W. W., (1947). High-efficiency counting of long-lived radioactive carbon as CO_2, Science **105,** 123.
Moseley, H. G. J. (1912). The number of β particles emitted in the transformation of radium, Proc. Roy. Soc. (A) **87,** 230.
Nadler, N. J. (1953). Quantitative estimation of radioactive isotopes by radioautography, Amer. J. Roentgenol. **70,** 814.
Nathan, D. G., Davidson, J. D., Waggoner, J. G., and Berlin, N. I. (1958). The counting of barium carbonate in a liquid scintillation spectrometer, J. Lab. and Clin. Med. **52,** 915.
Newell, R. R., Saunders, W., and Miller, E. (1952). Multichannel collimators for gamma-ray scanning with scintillation counters, Nucleonics **10,** No. 7, 36.
Nicholson, J. P., Wilson, C. W., and Newton, C. A. (1954). The distribution of radioiodine observed in thyroid disease by means of Geiger counters; its determination and significance, Amer. J. Roentgenol. **72,** 849.
Novey, T. B. (1950). RaDEF standard sources for beta-disintegration rate determinations, Rev. Sci. Instr. **21,** 280.
Paneth, F. A. (1950). Radioactive standards and units, Nature **166,** 931.
Pate, B. D., and Yaffe, L. (1955a). A new material and techniques for the fabrication and measurement of very thin film for use in 4π-counting, Can. J. Chem. **33,** 15.
Pate, B. D., and Yaffe, L. (1955b). Disintegration-rate determination by 4π-counting, Pt. I, Can. J. Chem. **33,** 610.

Pate, B. D., and Yaffe, L. (1955c). Disintegration-rate determination by 4π-counting, Pt. II. Source-mount absorption correction, Can. J. Chem. **33,** 929.
Pate, B. D., and Yaffe, L. (1955d). Disintegration-rate determination by 4π-counting, Pt. III. Absorption and scattering of radiation, Can. J. Chem. **33,** 1656.
Pate, B. D., and Yaffe, L. (1956). Disintegration-rate determination by 4π-counting, Pt. IV, self-absorption correction: general method and application to Ni^{63} β radiation, Can. J. Chem. **34,** 265.
Perry, W. E., Dale, J. W. G., and Pulfer, R. F. (1956). An ionization chamber for the secondary standardization and routine assay of radioactive materials. Memo. No. PH8/14/04—National Physical Laboratory, Teddington, England.
Piper, C. S. (1947). Soil and plant analysis (Interscience Publishers, Inc., New York, N.Y.).
Pochin, E. E. (1950). Investigation of thyroid function and disease with radioactive iodine, Lancet **2,** 41.
Pochin, E. E., Myant, N. B., Hilton, G., Honour, A. J., and Corbett, B. D. (1952). Indication for radioiodine treatment of thyroid carcinoma, Brit. Med. J. **2,** 1115.
Preiss, I. L., and Fink, R. W. (1957). Carrier free solution storage in glass, Nucleonics **15,** No. 10, 108.
Price, W. J. (1958). Nuclear radiation detection (McGraw-Hill Book Co., Inc., New York, N.Y.).
Prinzmetal, M., Corday, E., Spritzler, R. J., and Flieg, W. (1949). Radiocardiography and its clinical application, J.A.M.A. **139,** 617.
Pritchard, W. H., MacIntyre, W. J., and Moir, J. W. (1955). The determination of cardiac output by the dilution method without arterial sampling, J. Lab. Clin. Med. **46,** 939.
Putman, J. L. (1953). Limitations and extensions of the coincidence method for measuring the activity of beta-gamma emitters, Atomic Energy Research Establishment Report 1/M 26.
Quimby, E. H., Feitelberg, S., and Silver, S. (1958). Radioactive isotopes in clinical practice (Lea & Febiger, Philadelphia).
Raben, M. S., and Bloembergen, N. (1951). Determination of radioactivity by solution in a liquid scintillator, Sci. **114,** 363.
Reid, W. B., and Johns, H. E. (1958). An automatic brain scanner, Int. J. Appl. Rad. and Isotopes, **3,** 1.
Reines, F., Schuch, R. L., Cowan, C. L., Harrison, F. B., Anderson, E. C., and Hayes, F. B. (1953). Determination of total body radio activity using liquid scintillation detectors, Nature **172,** 521.
Rejali, A. M., MacIntyre, W. J., and Friedell, H. L. (1958). A radioisotope method of visualization of blood pools, Amer. J. Roentgenol. **79,** 129.
Rieck, H. G., Myers, I. T., and Palmer, R. F. (1956). Tritiated water standard, Rad. Research **4,** 451.
Robertson, J. S. (1957). Theory and use of tracers in determining transfer rates in biological systems, Physiological Reviews **37,** 133.
Rose, G., and Emery, E. W. (1951). Effects of solution composition in a G–M counter for liquid samples, Nucleonics **9,** No. 1, 5.
Rose, M. E., and Korff, S. A. (1941). An investigation of proportional counters I, Phys. Rev. **59,** 850.
Ross, D. A. (1959). Medical gamma-ray spectrometry, Oak Ridge Institute of Nuclear Studies Rept. No. 30.
Rossi, B. B., and Staub, H. H. (1949). Ionization chambers and counters (McGraw-Hill Book Co., Inc., New York, N.Y.).
Rossi, B. (1952). High energy particles (Prentice-Hall Inc., Englewood Cliffs, N.J.).

Roucayrol, J. C., Oberhausen, E., and Schubler, R. (1957). Emploi de scintillateurs liquides pour la mesure des activités béta molles sur papier-filtre avec une bonne sensibilité, Proc. First (UNESCO) Intern. Conf. on Radioisotopes in Scientific Research, **1,** 648.
Rundo, J. (1955). An Apparatus for the measurement of γ-radiation from the human body, J. Sci. Instr. **32,** 379.
Rutherford, E. (1905). Charge carried by the α and β rays of radium, Phil. Mag. [6] **10,** 193.
Rutherford, E., and Boltwood, B. B. (1905). The relative proportion of radium and uranium in radioactive minerals, Am. J. Science **20,** 55.
Schwebel, A., Isbell, H. S., and Karabinos, J. V. (1951). A rapid method for the measurement of carbon-14 in formamide solution, Science **113,** 465.
Schwebel, A., Isbell, H. S., and Moyer, J. D. (1954). Determination of carbon-14 in solutions of C^{14}-labelled materials by means of a proportional counter, J. Research NBS **53,** 221, RP2537.
Segré, E., (Editor) (1953). Experimental nuclear physics (John Wiley & Sons, Inc., New York, N.Y.).
Seliger, H. H. (1958a). Scintillation counting of beta emitters, Proc. of the First (UNESCO) Intern. Conf. on Radioisotopes in Scientific Research, **1,** 637 (Pergamon Press, London and New York).
Seliger, H. H. (1958b). Liquid scintillation counting, Proc. Symp. on measurements and standards of radioactivity, National Acad. of Sci., National Research Council Nuclear Science Ser. No. 24.
Seliger, H. H., and Agranoff, B. (1959). Solid scintillation counting of H^3 and C^{14} in paper chromatograms, Anal. Chem. **31,** 1607.
Seliger, H. H., Mann, W. B., and Cavallo, L. M. (1958). The average energy of sulfur-35 beta decay, J. Research NBS **60,** 447, RP2859.
Seliger, H. H., and Schwebel, A. (1954). Standardization of beta-emitting nuclides, Nucleonics **12,** No. 7, 54.
Seliger, H. H., and Ziegler, C. A. (1957). Thermal quenching in alpha- and gamma-excited liquid scintillators, J. Research NBS **58,** 125, RP2743.
Sharney, L., Wasserman, L. R., Schwartz, L., Tendler, D., and Vronman, L. (1958). Extension of the analysis of iron kinetics in terms of the multiple pool systems, Proc. 6th Intern. Cong. Intern. Soc. Hematology, Contrib. 228 P. Grume and Stratton.
Shore, L. G. (1949). Long-lived self-quenching counter filling, Rev. Sci. Instr. **20,** 956.
Shy, G. M., Bradley, R. B., and Matthews, W. B. (1958). External collimation detection of intracranial neoplasia with unstable nuclides (E. S. Livingstone Ltd., Edinburgh and London).
Sievert, R. M. (1951). Measurement of γ-radiation from the human body, Ark. Fys. **3,** 337.
Sinclair, W. K. (1950). Comparison of Geiger-counter and ion-chamber methods of measuring gamma radiation, Nucleonics, **7,** No. 6, 21.
Sinclair, W. K. (1951). Measurement and handling of radioactive materials for therapeutic use, Nucleonics **9,** No. 6, 35.
Sinclair, W. K., Abbatt, J. D., Farran, H. E. A., Harris, E. B., and Lamerton, L. F. (1956). A quantitative autoradiographic study of radioiodine distribution and dosage in human thyroid glands, Brit. J. Radiol. **29,** 36.
Sinclair, W. K., and Blondal, H. (1952). P^{32} beta sources for superficial therapy, Brit. J. Radiol. **25,** 360.
Sinclair, W. K., and Newberry, S. P. (1951). A direct reading meter for the measurement of highly active samples of gamma-emitting radioisotopes, J. Sci. Instr. **28,** 234.

Sinclair, W. K., Trott, N. G., and Belcher, E. H. (1954). The measurement of radioactive samples for clinical use, Brit. J. Radiol. **27,** 565.
Smith, B. C., and Quimby, E. H. (1945). Use of radioactive sodium in studies of circulation in patients with peripheral vascular ,disease Surg. Gynec. Obstet. **79,** 142.
Smith, D. B. (1953). 4π Geiger counters and counting techniques, Atomic Energy Research Establishment Rept. I/R 1210.
Smith, D. B. (1954). Absolute radioactivity measurements with 4π Geiger-Müller counters, Atomic Energy Research Establ. Rept. I/R 1527.
Smith, I. (1958). Chromatographic techniques (Intersci. Publishers, Inc., New York, N.Y.).
Smith, O. C. (1953). Inorganic chromatography (D. Van Ostrand Co., Inc., New York, N.Y.).
Soddy, F. (1914). The chemistry of the radio-elements (Longmans, Green and Co., London and New York).
Solomon, A. K. (1953). The kinetics of biological processes. Special problems connected with the use of tracers. Advances in Biological and Medical Physics **3** (Academic Press, Inc., New York, N.Y.).
Sommermeyer, K. (1952). Die Dosimetrie der Beta-Strahlung Radioaktiver Isotope in homogenen Substanzen, Z. Physik **133,** 201.
Sopp, T. E., Geyer, S. V., and Lehman, J. S. (1954). Economical scintillation scanner, Nucleonics **13,** No. 12, 49.
Stanley, M. M., and Astwood, E. B. (1947). Determination of relative activities of anti-thyroid compounds in man using radioactive iodine, Endocrinology **41,** 66.
Steinberg, D. (1958). Radioassay of carbon–14 in aqueous solutions using a liquid scintillation spectrometer, Nature **182,** 740.
Steinberg, D. (1959). Radioassay of aqueous solutions mixed with solid crystalline fluors, Nature, **183,** 1253.
Steyn, J. (1956). Absolute standardization of beta-emitting isotopes with a liquid scintillation counter, Proc. Phys. Soc. (A) **69,** 865.
Steyn, J., and Haasbroeck, F. J. (1958). The application of internal liquid scintillation counting to a $4\pi\beta-\gamma$ coincidence method for the absolute standardization of radioactive nuclides, Second United Nations Intern. Conf. on the Peaceful Uses of Atomic Energy, P/1104.
Stirrett, L. A., Yuhl, E. T., and Libby, R. I. (1953). New technique for diagnosis of carcinoma metastatic to the liver, Surg. Gynec. Obstet. **96,** 210.
Stirrett, L. A., and Yuhl, E. T. (1953). Clinical evaluation of hepatic radioactivity survey, Ann. Surg. **138,** 857.
Strong, J. (1943). Procedures in experimental physics (Prentice-Hall Inc., New York, N.Y.).
Strain, H. H. (1945). Chromatographic adsorption analysis (Interscience Publishers, Inc., New York, N.Y.).
Strain, H. H., and Murphy, G. W. (1952). Chromatography, Anal. Chem. **24,** 50.
Sweet, W. H., and Brownell, G. L. (1955). Localization of intracranial lesions by scanning with positron emitting arsenic, J. Amer. Med. Assoc., **157,** 1183.
Szilvasi, A. J. D., and Whyte, G. N. (1959). The energy response of a victoreen condenser ionization chamber, Physics in Medicine and Biology **3,** 207.
Taplin, G. V., Meredith, O. M., Jr., Kade, H., Westover, J. L., Hanse, R. A., and Bennett, L. R. (1955). The radioactive (I^{131} Labelled) rose Bengal liver uptake-excretion test. Its use in the evaluation of hepatic function, Intern. Conf. on Peaceful Uses of Atomic Energy, July 1, 1955.

Taplin, G. V., Meredith, O. M., Jr., Kade, H., and Winter, C. C. (1956). The radioisotope renogram. An external test for individual kidney function and upper urinary tract patency, J. Lab. Clin. Med. **48,** 886.
Toennies, G., and Kolb, J. J. (1951). Techniques and reagents for paper chromatography, Anal. Chem. **23,** 823.
Tolbert, B. M. (1956). Ionization chamber assay of radioactive gases U.S. Atomic Energy Commission Report UCRL–3499.
Tolbert, B. M. (1958). Tritium measurement using ionization chambers, Proc. Symp. Advances in Tracer Applications of Tritium.
Valentine, J. M., and Curran, S. C. (1958). Average energy expenditure per ion pair in gases and gas mixtures, Rep. Progr. Phys. **21,** 1.
Van Dilla, M. A., Schuch, R. L., and Anderson, E. C. (1954). K–9: A large 4π gamma-ray detector, Nucleonics **12,** No. 9, 22.
Van Slyke, D. D., Plazin, J., and Weisiger, J. R. (1951). Reagents for the Van Slyke-Folch wet carbon combustion, J. Biol. Chem. **191,** 299.
Veall, N. (1948). A Geiger-Müller counter for assaying the beta ray activity of liquids, Brit. J. Radiol. **21,** 347.
Veall, N., and Vetter, H. (1952). An apparatus for the rapid estimation of tracer quantities of radioactive isotopes in excreta, Brit. J. Radiol. **25,** 85.
Veal, N., and Vetter, H. (1958). Radioisotope techniques in clinical research and diagnosis (Butterworth & Co., London).
Verly, W. G., Bricteux-Grégoire, S., Koch, G., and Dewey, E. (1958). Windowless flow Geiger counters and the measurement of the soft beta activity of thick solid samples, Proc. of the Second United Nations Intern. Conf. on the Peaceful Uses of Atomic Energy, **21,** 131.
Wagner, C. D., and Guinn, V. P. (1955). For low specific activity; use scintillation counting, Nucleonics **13,** No. 10, 56.
Walton, R. J., and Sinclair, W. K. (1952). Intracavitary erradiation with radioactive colloidal gold in the palliative treatment of malignant pleural and peritoneal effusions, Brit. Med. Bull. **8,** 165.
Weil, H., and Williams, T. I. (1950). History of chromatography, Nature **166,** 1000.
Weiss, J., and Bernstein, W. (1955). Energy required to produce one ion pair for several gases, Phys. Rev. **98,** 1828.
Weidenbeck, M. L. (1947). The absolute strength of radioactive sources, Phys. Rev. **72,** 974.
Wien, W. (1903). Über die Selbstelektrisierung des Radiums und die Intensität der von ihm ausgesandten Strahlen, Phys. Z. **4,** 624.
Wilkinson, D. H. (1949). Ionization chambers and counters (McGraw-Hill Book Co., Inc., New York, N.Y.).
Wilkinson, D. H. (1950). Ionization chambers and counters (Cambridge University Press).
Williams, R. J. (1951). Biochemical institute studies, IV, individual metabolic patterns and human disease. An exploratory study utilizing predominantly paper chromatographic methods, University of Texas Publ. No. 5109, May 1, 1951.
Wilson, J. N. (1940). A theory of chromatography, J. Amer. Chem. Soc. **62,** 1583.
Wilzbach, K. E., Van Dyken, A. R., and Kaplan, L. (1954). Determination of Tritium by Ion Current Measurement, Anal. Chem. **26,** 880.
Wisham, L. H., and Yalow, R. S. (1952). Some factors affecting the clearance of Na^{24} from human muscle, Amer. Heart J. **43,** 67.

Wright, P., Osborne, S. B., and Edmonds, Denise (1949). Measurement of the rate of venous blood-flow in the legs of women at term and in the puerperium using radioactive sodium, J. Obst. Gyn. Brit. Emp. **56,** 35.
Wright, P., Osborne, S. B., and Edmonds, Denise (1951). Effect of post operative bed rest and early ambulation on the rate of venous Blood flow, Lancet **6,** 22.
Yaffe, L., and Fishman, J. B. (1960). Self-absorption studies with a $4\pi\beta$ proportional flow counter, Proc. IAEA Symp. Radioactive Metrology.
Yagoda, H. (1949). Radioactive measurements with nuclear emulsions (John Wiley & Sons, Inc., New York, N.Y.).
Yuhl, E. T., and Stirrett, L. A. (1953). Clinical evaluation hepatic radioactivity survey Ann. Surgery, **138,** 857.
Yuhl, E. T., Stirrett, L. A., and Cassen, B. (1953). Use of colloidal Au-198 for obtaining scintigrams of the liver, Nucleonics **11,** No. 4, 54.
Yuhl, E. T., Stirrett, L. A., Hill, M. R., and Beal, J. M. (1953). The cholescintigram. A preliminary report, Surgery **34,** 724.
Zechmeister, L., and Cholnoky, L. (1941). Principles and practice of chromatography (John Wiley & Sons, Inc., New York, N.Y.).

U.S. GOVERNMENT PRINTING OFFICE: 1961